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Number of parous events affects the association between physical exercise and glycemic control among women with gestational diabetes mellitus: A prospective cohort study

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Abstract

Background: Multiparous women are at a higher risk of gestational diabetes mellitus (GDM) than primiparas. Physical activity during pregnancy has been shown to be beneficial for GDM, but there is little evidence on the association between physical activity and glycemic control among women with GDM, whether primiparas or multiparas. Thus, the objective of the present study was to examine the association between physical activity and glycemic control in women with GDM and to determine what, if any, effects result from number of parous events.
Methods: A prospective cohort of 1162 women with GDM was recruited, with 604 multiparas (51.98%). The general linear model was used to calculate the risk difference and its 95% confidence interval (95%CI) to quantify the impact of parous events on glycemic control in pregnancy as well as the association between physical activity time and glycemic control.
Results: Among 1162 women with GDM, the median daily activity time was 65 min (interquartile range (IQR): 45−90 min), and the abnormal plasma glucose (PG) percentage, calculated as number of abnormal PG tests divided by the total number of PG tests, was 40.00% (IQR: 22.22%−66.67%). The percentage of abnormal PG was stabilized and statistically lower with daily physical activity time exceeding 60 min among primiparas (IQR: 30.89%−44.43%) and exceeding 90 min among multiparas (ranged from 27.76% to 38.82%). After adjusting for potential confounders, primiparas tended to have a lower percentage of abnormal PG than do multiparas (rate difference = −0.39, 95%CI: −3.61 to 2.84). The same amount of physical activity time was significantly less effective for multiparas than for primiparas (trend p-value < 0.01).
Conclusion: In women with GDM, being multiparous is associated with less effective glycemic control through physical activity, such that multiparas need more physical activity to achieve glycemic control at a similar level to primiparas.

Keywords: Gestational diabetes mellitus; Glycemic control; Parous events; Physical activity

1. Introduction

Any degree of glucose intolerance with onset or first recognition during pregnancy is defined as gestational diabetes mellitus (GDM).[1] GDM is associated with an increased risk of adverse prenatal complications and birth outcomes for both mothers and infants. GDM of any severity increases the risk of fetal macrosomia, neonatal hypoglycemia, jaundice, polycythemia, preterm birth, stillbirth, obesity, glucose intolerance, diabetes in late adolescence in children, and the risk of type 2 diabetes in mothers after birth.[1−3] The reported prevalence of GDM has varied from 2% to 32% across the world, and a recent study in China showed that the prevalence of GDM has increased there from 14% to 21%.[4−6] GDM has been a

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challenge for public health globally due to persistent risk factors, including unchanged lifestyle and imbalanced diet.[1] Given that a 3-child policy has recently been implemented in China, and given the continuing rapid growth of global population,[7] it is likely that the prevalence of GDM worldwide will continue to increase.

Successful management of GDM is urgently needed to avoid its severe adverse outcomes. The primary objective of GDM management is to achieve optimal glucose control so as to improve pregnancy outcomes and the well-being of mothers and children.[1] The GDM quintet management model has recommended 5 key interventions, including exercise, diet, maternal education, pharmacology, and fetal health evaluation.[1] Physical exercise has been proven to be an effective intervention for glucose control during pregnancy.[8] Updated recommendations from the American College of Obstetricians and Gynecologists and Canadian Society for Exercise Physiology are for at least 150 min of moderate-intensity physical activity each week for pregnant women without contraindication; however, due to low-quality evidence, a different recommendation was made for women with GDM.[9,10] The specific guideline on physical exercise for women with GDM was 30−60 min of moderate-intensity exercise, 3 times per week during pregnancy.[10] In a previous study, physical exercise times of more than 60 min per day were found to be associated with a lower percentage of abnormal plasma glucose (PG) among women with GDM.[11] Presently, evidence on the optimal amount of physical exercise needed to curb elevated glucose levels among women with GDM remains limited.

Previous studies have shown multiparous women to be at a higher risk of GDM and recurrence of GDM during their later pregnancies.[12] Wagan et al.[13] has reported that women with higher maternal age, multiparity, and previous GDM history have increased risk of GDM, and GDM women with advanced age had higher percentage of abnormal PG tests.[11] In general, multiparity in pregnant woman predicts a higher maternal age and a potential previous GDM history, so multiparous women with GDM are prone to a higher risk of poor glucose control than primiparous women. However, no study has been conducted to test this hypothesis. In addition, research has shown that physical exercise is effective in glucose control.[8,11] If multiparous women with GDM do have poor glucose control, as hypothesized, they may require longer physical exercise time than primiparous women to achieve the same level of glycemic control. To date, however, there is a lack of longitudinal studies investigating the relationship between physical exercise time and glucose control in both multiparous and primiparous women. Obtaining an answer to this question is important because it will provide evidence for the specific volume of physical exercise needed to prescribe for GDM women.

In this study, we set out to examine the association between parous events and glucose control, to examine the association between physical exercise and glucose control, and to explore any differences due to the number of parous events on the association between physical exercise and glucose control in a cohort of GDM women in Shanghai, China. We hypothesized that multiparous women were at a higher risk of poor glucose control than were primiparous women and that longer physical exercise time would be required for multiparous than for primiparous women to achieve the same level of glycemic control.

2. Methods

2.1. Study design and participants

This was a prospective cohort study conducted among women with GDM meant to explore the impact of parous events on the association between glycemic control and physical activity during pregnancy. Detailed information regarding sample size estimation and the recruitment process for women with GDM is available in previously published work.[11] The primary purpose of this research with the cohort of GDM women was to evaluate the impact of physical activity on preterm birth, adverse perinatal outcomes, and type 2 diabetes after delivery. Women with GDM verified by a diagnostic 75 g oral glucose tolerance test (OGTT) at gestational Weeks 24−28 were recruited from the Songjiang Maternal and Children's Health-care Hospital, District of Songjiang, Shanghai, China, from August 2019 to August 2020.

Eligible participants were assessed in early pregnancy (24−28 weeks of gestation) during their antenatal care. Inclusion criteria were: (a) aged 18−45 years; (b) currently living in the District of Songjiang without any migration plan in the next 2 years; (c) with gestation of 24−28 weeks; (d) singleton pregnancy; (e) without preexisting health conditions, such as cancers, ischemic heart diseases; (f) GDM confirmed by a diagnostic 75 g OGTT (0-h (fasting) PG $\geq$ 5.10 mmol/L, 1-h PG $\geq$ 10.00 mmol/L, and 2-h PG $\geq$ 8.50 mmol/L); (g) being able to read and sign the informed consent form. An additional criterion was that the information for each participant should be complete. A total of 1162 women with GDM were finally enrolled in the study.

Ethics approval was authorized by Songjiang Maternal and Children's Health-care Hospital Institution Review Board (IRB#-2019-12-003). Informed consent was provided by each participant before the questionnaire interview. This study was conducted following the Helsinki Declaration and registered in the Chinese Clinical Trial Registry (ChiCTR2000028832).

2.2. Data collection

There were 2 data sources in this cohort study: one from the health records in the hospital and the other from face-to-face interviews. Data extracted from the health records included demographic information (age, education, occupation, residency status, and individual monthly income), pregnancy and childbirth history, routine antenatal checkup information, height and weight before pregnancy, PG test records, and newborn delivery information (gestational week, mode of delivery, gender and birth weight of baby, and information about any postpartum hemorrhage). Face-to-face interviews were conducted by trained nurses after the delivery in the hospital, and investigations focused on performance of 20 types of physical activity during pregnancy (walking, house cleaning, stationary bike riding, jogging, swimming, climbing stairs, Tai Chi, soft gymnastics, yoga, oxygen dance, *etc*.), and information about the frequency and duration of each physical activity with moderate intensity (a normal physical effort that made pregnant women breathe slightly harder and made their heart beat a little faster to a level less than 60%−80% of age-predicted maximum maternal heart rate and usually not exceeding 140 beats per minute)[10,11] undertaken during gestational Weeks 27−40.

Records with missing values were flagged and double-checked by reference to the original paper records. Each nurse received training to ensure accuracy. All data were de-identified and thus could not be linked to any specific individual. Once data were collected, they were encrypted and accessed only by the principal investigators.

2.3. Definitions and measurements

In this study, the International Association of Diabetes and Pregnancy Study Group criteria were used to diagnosis GDM,[14] and GDM was verified by a diagnostic 75 g OGTT at gestational Weeks 24−28 when any one of the following values was met or exceeded: fasting PG (0-h) $\geq$ 5.10 mmol/L, 1-h PG $\geq$ 10.00 mmol/L, and 2-h PG $\geq$ 8.50 mmol/L.[14] Glycemic control was evaluated during routine antenatal checkup in gestational Weeks 27−28, Weeks 29−30, Weeks 31−32, Weeks 33−34, Weeks 35−36, Weeks 37−38, and Weeks 39−40 (pre-birth) by the percentage of abnormal PG. An abnormal PG was defined as the morning PG $\geq$ 5.10 mmol/L with over 10 overnight fasting or (and) $\geq$8.5 mmol/L within 2 h following a standard breakfast in each routine antenatal checkup after the confirmation of GDM.[15,16] The percentage of abnormal PG was calculated as number of abnormal PG tests divided by the total number of PG tests. A higher level of abnormal PG percentage was considered to indicate worse glycemic control.

Amount of physical activity with moderate intensity was assessed by the reported total daily activity times as well as the total weekly activity times. First, physical activity time was calculated as monthly activity frequency multiplied by the average duration of each activity, then divided by 30 days. Thereafter, the 20 types of physical activity times were combined to provide the total daily time of physical activity with moderate intensity for each participant. For example, if a woman with GDM reported 2 types of moderate-intensity physical activity (e.g., riding a bicycle for work and line dancing) during the gestation Weeks 27−40, and the frequency and duration were 15 times per month and 30 min each time on average for bicycle riding and 10 times per month and 20 min each time on average for line dancing, then the total daily activity time was 21.67 min ($(15 \times 30 + 10 \times 20)/30$). We then classified participants into dichotomous groups according to their total daily activity times: "<30 min/day" and "≥30 min/day", "<60 min/day" and "≥60 min/day", "<90 min/day" and "≥90 min/day", and "<120 min/day" and "≥120 min/day". We also classified the women in the cohort according to their total daily physical activity times: "<60 min/day", "60−89 min/day", "90−119 min/day", and "≥120 min/day".

In this study, parity of participants was dichotomized into multiparous and primiparous. A multipara was defined as a woman who had given birth at least twice to an infant, liveborn or not, weighing 500 g or more or having an estimated length of gestation of at least 20 weeks. A primipara was defined as a woman who was giving birth for the first time.

Body mass index (kg/m^2) before pregnancy was classified as "<18.5", "18.5−23.9", ">23.9−27.9", and ">27.9". Weight gain (kg) in gestation was the difference between pre-birth body weight and pre-pregnancy body weight. Age (year) was categorized into 4 groups: "18−25", "26−30", "31−35", and "36−45". Education was documented as the completed years of schooling and classified into 3 categories: 6−9 years (primary or junior high school), 10−12 years (senior high school), and >12 years (college and above). Individual monthly income (RMB) was categorized into 4 groups: "<3000", "3000−5000", "5001−10,000", and ">10,000" (which could be converted into US dollars with an exchange rate of 6.5: "<462", "462−770", "771−1538", and ">1538").

2.4. Statistical analysis

Means and standard deviations were calculated for normally distributed quantitative data, and the median and interquartile range (IQR) for skewed data. Qualitative data were described with counts and percentages. χ^2 tests were applied to examine the percentage differences between primiparous and multiparous GDM women with different demographic characteristics, physical activity during pregnancy, body mass index, hypertension, and diabetes before pregnancy. Student's t tests and Mann−Whitney U tests were applied to assess the difference between normally distributed data and skewed data, respectively. Figures were produced to describe the association between daily physical activity times and the percentage of abnormal PG within the different stratum of parous events.

In light of the continuous variable feature of the abnormal PG percentage, we applied the general linear model (GLM) to calculate the risk difference and its 95% confidence interval (95%CI) to enable evaluation of the impact of parity and physical activity on glycemic control during pregnancy and the modification of the effect of physical activity on glycemic control by number of parous events. Potential confounders adjusted in multi-variable regression models were identified by the directed acyclic graphs.[17] The linear trend of physical activity time and glucose control within each stratum of parity was evaluated with a Wald test by assigning the median value to each category of physical activity time, and the variable was treated as a continuous variable.

Modification of the effect of physical activity on glycemic control was evaluated on an additive scale through 3 steps according to the procedure described by Knol et al.[18] First, the reference group was set as the group of women with physical activity time < 60 min/day, and who were also multiparous. Second, risk differences (RDs) and 95%CI were presented for physical activity time groups within the strata of primiparous and multiparous by adjusting potential confounders. Third, effect modifications were calculated on an additive scale with 95%CI and p values. For example, if physical activity time increased from the level of "<60 min/day" to the level of "90−119 min/day", then the effect modification by parity can be estimated as follows: Δ = (Effect of stratum ("90−119 min/day" and primiparous) − Effect of stratum ("<60 min/day" and primiparous)) − (Effect of stratum ("90−119 min/day" and multiparous) − Effect of stratum ("<60 min/day" and multiparous)). If the value Δ is positive, then it means that the effect of physical activity time on glycemic control among primiparous women was weaker than that among multiparous women. Otherwise, if the value is negative, the effect of physical activity time on glycemic control among primiparous women was better than that among multiparous women.

In this study, SAS software (Version 9.4; SAS Institute, Cary, NC, USA) was applied in the statistical analysis. Point estimate and 95%CIs of RDs were taken into consideration to justify the association as well,[19] and a p value of less than 0.05 (2-tailed) was considered statistically significant.

3. Results

A total of 1162 GDM women were enrolled, with 558 primiparous women (48.02%) and 604 multiparous women (51.98%), and the overall mean age was 30.51 ± 4.32 years. Approximately 60% of the women had an education of college level and above (>12 years), and more than three-quarters earned an individual income more than RMB 5000 (USD 770) per month. Around one-third were overweight or obese before pregnancy. The median value of weight gain in gestation was 9.60 kg (IQR: 7.00−12.30) (Table 1). The median daily activity time was 65 min (IQR: 45−90), with 38.9% having a daily physical activity time less than 60 min and 7.8% having a daily physical activity time over 2 h. Both multiparous and primiparous women with GDM attended a similar number of times for antenatal checkups during pregnancy. Multiparous women with GDM were older, with lower levels of advanced education and monthly income, and they had less daily physical activity time than that observed among primiparous women (60 min *vs.* 75 min, $p < 0.001$) (Tables 1 and 2).

3.1. Abnormal PG percentage within subgroups of parity and physical activity time

The median value of abnormal PG percentage in women with GDM was 40.00% (IQR: 22.22%−66.67%), and the difference in abnormal PG percentage during the entire antenatal period between primiparous and multiparous women was not statistically significant (37.50% *vs.* 40.00%, $p = 0.801$)

Table 1
The demographic features among women with GDM ($n = 1162$).

Variable	Participants ($n = 1162$)	Primipara women ($n = 558$)	Multipara women ($n = 604$)	t/χ^2	p
Age (year)[a]	30.51 ± 4.32	28.62 ± 3.82	32.26 ± 4.01	−15.81	0.000
Age group (year)[b]				207.97	0.000
18−25	139 (11.96)	116 (20.79)	23 (3.81)		
26−30	459 (39.50)	285 (51.08)	174 (28.81)		
31−35	412 (35.46)	131 (23.48)	281 (46.52)		
36−45	152 (13.08)	26 (4.66)	126 (20.86)		
Education[b]				68.24	0.000
Primary/junior high	241 (20.74)	64 (11.47)	177 (29.30)		
Senior high	223 (19.19)	97 (17.38)	126 (20.86)		
College and above	698 (60.07)	397 (71.15)	301 (49.83)		
Individual monthly income (RMB)[b]				20.61	0.000
<3000 (USD < 462)	49 (4.22)	18 (3.23)	31 (5.13)		
3000−5000 (USD 462−770)	224 (19.28)	81 (14.52)	143 (23.68)		
5001−10,000 (USD 771−1538)	605 (52.07)	306 (54.84)	299 (49.50)		
>10,000 (USD >1538)	284 (24.44)	153 (27.42)	131 (21.69)		
Residency status[b]				23.93	0.000
Local resident	371 (31.93)	217 (38.89)	154 (25.50)		
Non-local resident	791 (68.07)	341 (61.11)	450 (74.50)		
BMI (kg/m^2) before pregnancy[b]				4.39	0.221
<18.5 (lower body weight)	53 (4.56)	28 (5.02)	25 (4.14)		
18.5−23.9 (normal body weight)	702 (60.41)	351 (62.90)	351 (58.11)		
> 23.9−27.9 (overweight)	317 (27.28)	141 (25.27)	176 (29.14)		
>27.9 (obesity)	90 (7.75)	38 (6.81)	52 (8.61)		
Hypertension before pregnancy[b,c]				–	0.271
Yes	7 (0.60)	5 (0.90)	2 (0.33)		
No	1155 (99.40)	553 (99.10)	602 (99.67)		
Diabetes before pregnancy[b,c]				–	0.626
Yes	4 (0.34)	1 (0.18)	3 (0.50)		
No	1158 (99.66)	557 (99.82)	601 (99.50)		
Weight gain in gestation (kg)[d]	9.60 (7.00−12.30)	9.90 (7.20−13.00)	9.30 (7.00−12.05)	4.81	0.028

[a] Mean ± SD.
[b] n (%).
[c] Fisher exact text.
[d] Median (interquartile range).
Abbreviations: BMI = body mass index; GDM = gestational diabetes mellitus.

Table 2
Routine antenatal checkup and physical activity condition among women with GDM ($n = 1162$).

Variable	Participants ($n = 1162$)	Primipara women ($n = 558$)	Multipara women ($n = 604$)	χ^2	p
Times of antenatal checkup[a]	8.00 (7.00−9.00)	8.00 (7.00−9.00)	8.00 (6.00−9.00)	0.26	0.612
Percentage of abnormal PG in total[a]	40.00 (22.22−66.67)	37.50 (22.22−66.67)	40.00 (22.22−66.67)	0.06	0.801
Percentage of abnormal PG in each test[b]					
Gestational diabetes mellitus identification ($n = 1162$)	1162 (100.00)	558 (100.00)	604 (100.00)	0.00	1.00
First following checkup ($n = 1160$)	542 (46.72)	262 (47.04)	280 (46.43)	0.04	0.837
Second following checkup ($n = 1150$)	521 (45.30)	250 (45.29)	271 (45.32)	0.01	0.992
Third following checkup ($n = 1113$)	467 (41.96)	215 (40.06)	252 (43.75)	1.57	0.209
Fourth following checkup ($n = 1030$)	396 (38.45)	177 (35.19)	219 (41.56)	4.41	0.036
Fifth following checkup ($n = 882$)	338 (38.32)	172 (39.18)	166 (37.47)	0.27	0.602
Sixth following checkup ($n = 696$)	251 (36.06)	126 (36.52)	125 (35.61)	0.06	0.803
Seventh following checkup ($n = 378$)	136 (35.98)	60 (35.09)	76 (36.71)	0.11	0.743
Eighth following checkup (pre-birth, $n = 1162$)	127 (10.93)	74 (13.26)	53 (8.77)	5.99	0.015
Types of physical activity[a]	3.00 (2.00−4.00)	3.00 (2.00−4.00)	3.00 (2.00−5.00)	31.15	0.000
Daily physical activity time (min/day)[a]	65.00 (45.00−90.00)	60.00 (45.00−80.00)	75.00 (50.00−95.00)	27.55	0.000
Groups of daily physical activity time[b]				33.22	0.000
<60 min/day	453 (38.98)	247 (44.27)	206 (34.11)		
60−89 min/day	388 (33.39)	200 (35.84)	188 (31.13)		
> 89−119 min/day	230 (19.79)	82 (14.70)	148 (24.50)		
>119 min/day	91 (7.83)	29 (5.20)	62 (10.26)		
Percentage of physical activity <30 min/day[b]	57 (4.91)	26 (4.66)	31 (5.13)	0.14	0.709
Percentage of physical activity <60 min/day[b]	453 (38.98)	247 (44.27)	206 (34.11)	12.59	0.000
Percentage of physical activity <90 min/day[b]	841 (72.38)	447 (80.11)	394 (65.23)	32.10	0.000
Percentage of physical activity <120 min/day[b]	1071 (92.17)	529 (94.80)	542 (89.74)	10.32	0.001

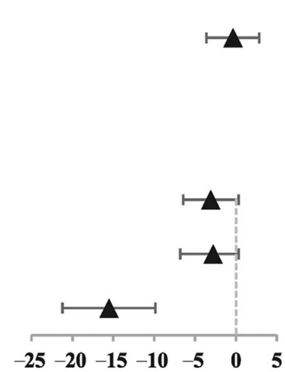
Note: Data are shown as [a] median (interquartile range) and [b] n (%).
Abbreviations: GDM = gestational diabetes mellitus; PG = plasma glucose.

(Table 2). In routine antenatal checkups, the abnormal PG percentage was higher in the second trimester while lower in the third trimester among multiparous as opposed to primiparous GDM women, but the difference was only statistically significant at the fourth and eighth antenatal checkups (Table 2).

In Table 3, the general linear model, after having adjusted for potential confounders, indicated that while primiparous

Table 3
Separate effects of physical activity time as well as parity on the percentage of abnormal plasma glucose test times during pregnancy among women with GDM ($n = 1162$).

Item	n (mean)	RD (95%CI of RD)
Parity [a]		
Multipara	604 (44.77)	0.0 (Ref)
Primipara	558 (44.45)	−0.39 (−3.61 to 2.84)
Physical activity groups [b]		
<60 min/day	453 (47.44)	0.0 (Ref)
60–89 min/day	388 (44.05)	−3.07 (−6.46 to 0.33)
90–119 min/day	230 (44.94)	−2.79 (−6.80 to 1.23)
≥120 min/day	91 (32.13)	−15.54 (−21.23 to −9.85)



[a] Adjusted covariate includes age.
[b] Adjusted covariates include age, individual monthly income, education, and body mass index before pregnancy. And the trend analysis was conducted for physical activity time groups with $p < 0.001$.
Abbreviations: 95%CI = 95% confidence interval; GDM = gestational diabetes mellitus; RD = risk difference.

GDM women tended to have a lower percentage of abnormal PG than did multiparous GDM women, the difference was not significant, as the p value was greater than 0.05.

Fig. 1 shows a downward trend in the average percentage of abnormal PG as physical activity time is increased, whether in the whole population or in each stratum of parity. Table 3 data shows that there was a negative association between physical activity time and the percentage of abnormal PG (the p value for trend was less than 0.001), which indicates that GDM women with less physical activity time tend to have a higher percentage of abnormal PG. Moreover, the percentage of abnormal PG tended to stabilize and was statistically lower when daily physical activity time exceeded 60 min among primiparous GDM women (ranged from 30.89% to 44.43%) and exceeded 90 min among multiparous GDM women (ranged from 27.76% to 38.82%) (Fig. 1 and Supplementary Fig. 1). In this study, Fig. 2 shows the estimated percentages of abnormal PG within each stratum of parity, after adjusting for potential confounders, and indicates that the negative association between physical activity time and percentage of abnormal PG was consistent across the strata of parity (Fig. 2).

3.2. *Parous events difference in the association between physical activity time and abnormal PG percentage*

Table 4 shows the RDs and 95%CIs within each stratum and the effect modification of physical activity time on abnormal PG percentage by parous events. In comparison with daily physical activity time <60 min, the percentage of abnormal PG decreased with the elevated times of daily physical activity, both for primiparous women and multiparous women. Setting multiparous women with GDM who had physical activity time of <60 min/day as the reference, the effect modification by parity was −4.02 (95%CI: −12.04 to 4.00) for the group with activity time of 90−119 min/day. This indicates that the estimated percentage of abnormal PG for primiparous women in the group with physical activity time of 90−119 min/day was lower than the estimated percentage of abnormal PG for multiparous women in the group with physical activity time of 90−119 min/day, meaning there was a negative effect modification from primiparous women to multiparous women based on an additive scale. Negative effect modifications were identified in other strata of physical activity time as well, including −8.14 (95%CI: −14.86 to −1.43) for 60−89 min/day and −11.57 (95%CI: −23.30 to 0.16) for ≥120 min/day.

3.3. *Sensitivity analysis*

We performed a sensitivity analysis to examine the effect modification of parity on glucose control among GDM women during pregnancy. Percentages of abnormal PG were treated dichotomously according to different cutoff values, including 20%, 40%, and 60%, and logistic regression models were applied to test the association between parous events and the percentage of abnormal PG. Results suggested that the negative effect modifications of parity on the association between physical activity time and percentage of abnormal PG were consistent across different scenarios (Supplementary Table 1).

4. Discussion

GDM is 1 of the most common complications of pregnancy, and glycemic control by physical activity is critical for the health of women with GDM.[11,12] In this study, we observed that the number of parous events negatively influenced glucose control among women with GDM during their pregnancy. Multiparous women had a higher percentage of abnormal PG (40.0%) compared to primiparous women (37.5%), and parity was observed to negatively modify the effect of physical activity time on glucose control among GDM women. The effect of physical activity time on glucose control within the stratum of primiparous women was stronger than that within the stratum of multiparous women. The percentage of abnormal PG was statistically lower when daily physical activity time exceeded 60 min among primiparous women and when it exceeded 90 min among multiparous women. The association between longer physical activity times and lower percentage of abnormal PG among GDM women might be explained by the fact that physical exercise may actively affect insulin resistance in patients with GDM.[20] Insulin resistance can increase energy supply for lipid oxidation, promote glucose phosphorylation in muscle cells, and transform blood sugar to myosin to make glucose more stable so as to maintain the balance between glucose and insulin secretion.[21]

This study found that multiparous women with GDM were at a higher risk of poor glucose control during pregnancy than primiparous women with GDM. The association between parity and GDM has been investigated in other studies. One study indicated that multiparous women were more likely to have GDM.[12] Previous studies, including meta-analyses have indicated that women with an increasing number of births were associated with increasing recurrence of GDM.[22−24] One possible mechanism for the association between parous events and glucose control among GDM women is that these episodes of insulin resistance may contribute to the decline in β-cell function since each pregnancy is characterized by an episode of insulin resistance.[25] In addition, the effect of parity maybe also due to the fact that mothers who have experienced previous episodes of pregnancy could also have affected insulin sensitivity and glucose metabolism and were slightly more overweight. Findings from the present study provide further evidence that multiparous GDM women were susceptible to poor glucose control, and they extend the research by showing that more physical activity time (at least 90 min of activity with moderate intensity each day) is needed to obtain a beneficial response in this vulnerable population.

Physical activity among multiparous women was observed to be less effective than among primiparous women. To our knowledge, this study was the first to investigate differences due to parity in the association between physical activity time and glucose control among women with GDM. Previous studies have demonstrated that parity modifies the effect of air pollution on GDM,[2] a finding which could strengthen the

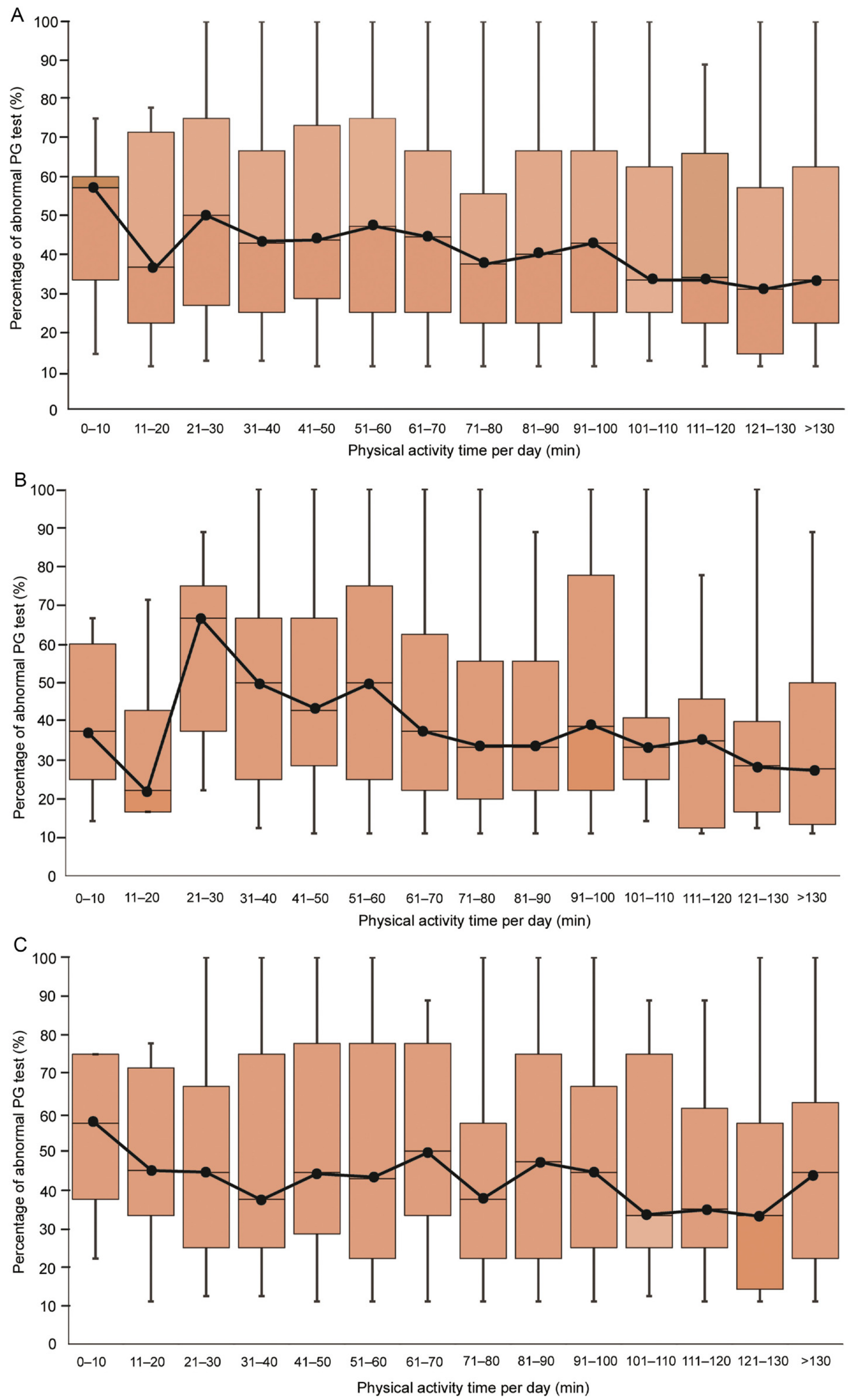


Fig. 1. The box plot indicates a downward trend in the mean percentage of abnormal PG as physical activity time is increased in (A) all GDM women ($n = 1162$), (B) primipara GDM women ($n = 558$), and (C) multipara GDM women ($n = 604$). The percentage of abnormal PG tended to stabilize and was statistically lower when daily physical exercise time exceeded 60 min among primiparous GDM women (B), and when it exceeded 90 min among multiparous GDM women (C). The bold circle, bar, and the 2 parts of the column in the box plot means the median (P50), minimum (P0), maximum (P100), and the 25th percentile (P25) and the 75th percentile (P75) value of abnormal PG percentage in each physical exercise group. The *p*-value for trend was less than 0.01. GDM = gestational diabetes mellitus; PG = plasma glucose.

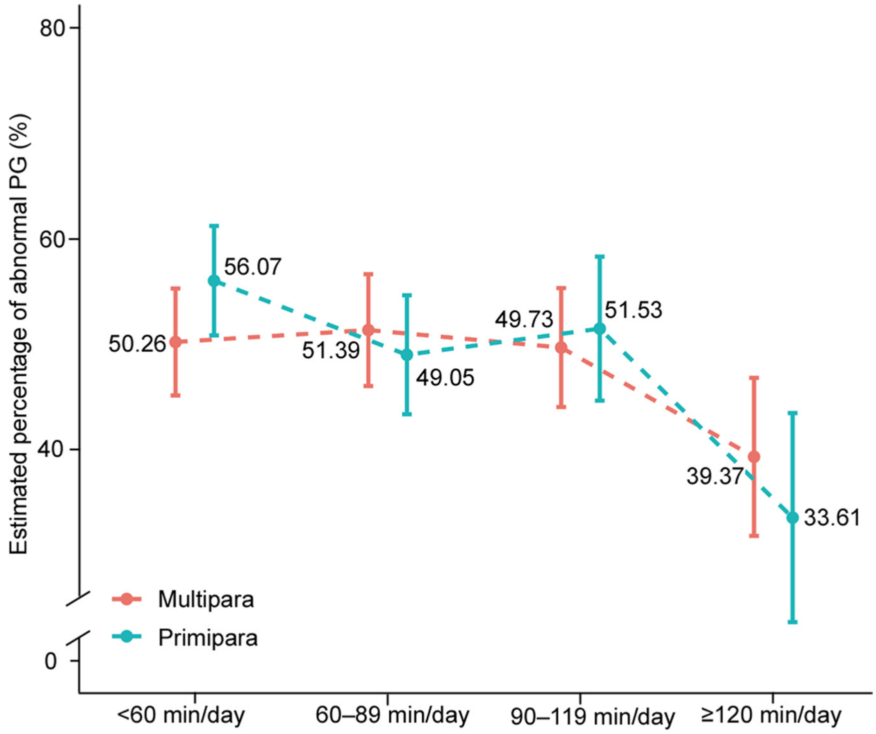
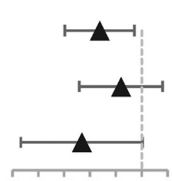


Fig. 2. Estimated percentage of abnormal PG within each stratum of physical activity group and parity with the adjustment of covariates of age, education, individual monthly income, and BMI before pregnancy. Physical activity time was negatively associated with the percentage of abnormal PG, and the association was consistent across the strata of parity. Data are shown as median and IQR (P25, P75). BMI = body mass index; PG = plasma glucose.

association between air pollution and GDM. This result is consistent with current findings, which have demonstrated that multiparous women are more likely to have a higher level of abnormal PG. It may be that the greater number of episodes of insulin resistance among multiparous women than among primiparous women with GDM means that more physical activity time is required for multiparas to achieve a similar effect to that achieved by primiparas. This result is important not only for understanding the mechanism but also for its public health implications. There is an elevated number of multiparous women worldwide, especially in China since the implementation of the 2-child policy and the recently announced 3-child policy.[7] Individualized recommendations for physical activity time for GDM women with different parity could be helpful for the prevention of GDM. Given the negative effect modification by the number of parous events, we recommend longer physical activity times for multiparous GDM women so as to achieve optimal glucose control. Referencing the 2019 Canadian guidelines for physical activity throughout pregnancy, which suggest at least 150 min of moderate intensity physical exercise per week for pregnant women,[1,10] we recommend that at least

Table 4
Modification of the effect of physical activity time on the percentage of abnormal plasma glucose test times during pregnancy by parities among gestational diabetes mellitus women ($n = 1162$).

Physical activity groups	Multipara		Primipara		Measure of effect modification on additive scale (95%CI)
	n (mean)	RD (95%CI)	*n* (mean)	RD (95%CI)	
<60 min/day	206 (45.95)	0.00 (Ref)	247 (48.69)	5.22 (0.31 to 6.42)	–
60–89 min/day	188 (46.50)	0.61 (−4.32 to 5.54)	200 (41.75)	−1.07 (−6.14 to 4.00)	−8.14 (−14.86 to −1.43)
90–119 min/day	148 (45.42)	−0.32 (−5.63 to 5.00)	82 (44.07)	−0.17 (−6.26 to 6.60)	−4.02 (−12.04 to 4.00)
≥120 min/day	62 (28.02)	−12.32 (−19.44 to −5.20)	29 (34.06)	−17.40 (−27.07 to −7.72)	−11.57 (−23.30 to 0.16)



Note: RDs were adjusted for age, education, individual monthly income, body mass index before pregnancy.
Abbreviations: 95%CI = 95% confidence interval; RD = risk difference.

60 min of moderate-intensity physical activity per week is needed for primiparous women with GDM, and at least 90 min moderate-intensity physical activity per week is needed for multiparas. Further, for currently primiparous women with GDM, the physical activity times that they engage in for their later pregnancies should be at a higher level than their current physical activity times, given the physical activity effect modification from parous events.

Twenty types of physical activity performed during pregnancy (such as walking, house cleaning, stationary riding, jogging, swimming, climbing stairs, Tai Chi, soft gymnastics, yoga, aerobic dance, *etc*.) were included in this study. According to our findings, and those of previously published researches,[9–11] we would recommend that other physical activity that involves aerobic and resistance exercise components, such as Pilates and aquatics with moderate intensity, should be considered for GDM women, whether primiparas or multiparas, under the supervision of health care professionals.

A major strength of the current study was the quantitative estimation of effect modification of parity on the association between physical activity time and glucose control, based on the availability of high-quality data from a prospective cohort of women with GDM. This study saw relatively less recall bias because information about pregnancy and childbirth history, as well as about morning PG levels (in a fasting state and at 2 h after breakfast), was extracted directly from the delivery records and routine antenatal checkup forms. Another strength of this study is that it used directed acyclic graphs to identify potential confounders and then adjusted for them in the general linear regression analysis, which ensured a relatively unbiased assessment of the association between physical activity times and the percentage of abnormal PG, as well as between parity and the percentage of abnormal PG.

This study also has some limitations. First, as a secondary data analysis from a cohort study, the sample size was not calculated specifically for the current study and was not sufficiently large for further analyses of effect modification. Second, the data for physical activity times were self-reported, which might induce report bias for the exposure assessment. Third, not all potential confounders were collected, including daily dietary information and other environmental factors, which may mean that the study did not control for all potential confounds. Fourth, a detailed diet assessment of women with GDM was not performed, so although we assumed that there was not a big difference in diet among women with GDM, we still could not investigate and analyze the combined effect of diet and physical activity. Fifth, all participants in this study were Chinese, which may limit the generalization of findings to different groups. This feature should be considered in follow-up studies, and future studies conducted in different countries are warranted.

5. Conclusion

In women with GDM, being multiparous was found to be associated with less effective glucose control through physical activity. Consequently, multiparas need a higher activity dose for effective management of GDM, so as to achieve a similar level of glucose control to women with GDM who are having their first child. Future interventions to optimize glucose control among women with GDM should consider their number of parous events.

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Authors' contributions

RW, BL, and JH participated in study design; FY and JC conducted the study and drafted the paper; TS, YQ, HL, YT, and QY participated in field work; and RA revised the paper. All authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

Competing interests

The authors declare that they have no competing interests.

Supplementary materials

Supplementary materials associated with this article can be found in the online version at doi:10.1016/j.jshs.2022.03.005.

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