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Original article

Gestational weight gain is associated with delayed onset of lactogenesis in the TMCHC study: A prospective cohort study

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SUMMARY

Background & aims: Delayed onset of lactogenesis II (OL) negatively affects breastfeeding and consequently, the health of the newborn. Few studies have examined the association between gestational weight gain (GWG) throughout pregnancy and risk of delayed OL.

Methods: We used data from a prospective cohort study in Wuhan of China, which enrolled pregnant women at 8–16 weeks of gestation and followed-up regularly. GWG was assessed by the last available weight measurement (LAWM) during pregnancy and the self-reported pre-pregnancy weight at enrollment. The outcome was delayed OL self-reported after 4 days postpartum. Odds ratios (ORs) and 95% confidence intervals (CIs) were derived from multivariate logistic regression.

Results: Delayed OL was reported by 18.4% of the 3282 participants. After adjustment for the demographic, clinical and breastfeeding characteristics, compared to the lowest quartile 1 of GWG, ORs (95% CIs) were 1.20 (0.91, 1.57) for quartile 2, 1.47 (1.13, 1.92) for quartile 3, and 1.42 (1.08, 1.86) for quartile 4 (*P* for trend = 0.006). When GWG was classified by the 2009 Institute of Medicine (IOM) guidelines, compared with women with adequate GWG, the adjusted ORs (95% CIs) were 0.82 (0.61, 1.10) for inadequate GWG, and 1.13 (0.93, 1.38) for excessive GWG.

Conclusions: Women with higher GWG throughout pregnancy are more likely to suffer from delayed OL in Chinese population.

1. Introduction

Onset of lactogenesis II (OL) is the initiation of copious milk secretion [1,2] and should occurs between 36 and 92 h postpartum, which is measured usually by maternal perception of breast hardness, fullness, or leakage of colostrum or breast milk [3,4]. The timing of OL is important for the success of breastfeeding and thus newborn health. The perception of OL more than 72 h postpartum is considered delayed OL. Previous studies have found that women experiencing delayed OL may be less able to sustain exclusive breastfeeding in the early postpartum period [5], which is also related to excess neonatal weight loss (≥10% of birth weight) [6] and early breastfeeding cessation [5,7,8].

Determinants of delayed OL have been studied and maternal adiposity before conception has been suggested to be an important risk factor [9–13]. Women who were overweight or obese pre-conception were found having a lower prolactin response to infant sucking [14], which is necessary for OL [1,15] and related to delayed OL. Fewer studies have focused on the association of GWG with delayed OL [6,11,12,16], and the Results were controversial. In a cohort study conducted in southeastern United States, GWG was positively associated with delayed OL among 216 women [12]. The Infant Feeding Practices Study II conducted in United States reported an increased risk of delayed OL by excessive GWG among

Abbreviations: GWG, gestational weigh gain; OL, onset of lactogenesis II; GDM, gestational diabetes mellitus; LAWM, the last available weight measurement.

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non-Hispanic white women, but not in other racial/ethnic groups [16]. However, a research conducted in California found no association between excessive GWG and delayed OL among 883 women with Gestational diabetes mellitus (GDM) [11]. Studies are needed to address the association among pregnant women given the increasing prevalence of excessive GWG.

Therefore, we analyzed data from a large birth cohort study in Wuhan, China, aiming to 1) investigate the incidence of delayed OL; 2) examine the association between GWG throughout pregnancy and delayed OL.

2. Materials and method

2.1. Study participants

This study was embedded in Tongji Maternal and Child Health Cohort (TMCHC) study, which is a prospective, observational investigation with pregnant women and their infants residing in Wuhan, Hubei province, central China. Its primary purpose is to examine the effect of maternal dietary and lifestyle factors on the health of pregnant women and their offspring [17]. The recruitment for the TMCHC study started in January 2013 and enrolled pregnant women from 8–16 gestational weeks who could read and talk in Chinese freely at their first antenatal visits. Women were excluded if they were younger than 18 y of age. All participants were furnished with written informed consent at enrollment. The study was approved by the Ethics Review Committee of Tongji Medical College, Huazhong University of Science and Technology (NO. 201302).

Participants in the present study were all from TMCHC, and the additional criteria were: (1) a singleton, live birth ≥37 week gestation; (2) initiated breastfeeding; (3) data available on GWG and OL, and (4) no separation of mother or infant >24 h.

2.2. Assessment of maternal BMI and GWG

Weight before pregnancy was self-reported and maternal height was measured by research personnel at enrollment. Weight was measured at the initial and follow-up prenatal visit, postpartum weight was also measured at day 1 postpartum in hospital. Maternal pre-pregnancy BMI was calculated as pre-pregnancy weight (in kg) divided by height squared (in m^2) and was categorized according to the Chinese adult BMI classification [18] as underweight (<18.5 kg/m^2), normal weight (18.5–23.9 kg/m^2), overweight (24.0–27.9 kg/m^2), and obese (≥28.0 kg/m^2). Postpartum BMI was calculated according postpartum weight measured.

GWG during pregnancy was defined as the difference between the last available weight measurement (LAWM) during pregnancy and the pre-pregnancy weight. The LAWM was measured on admission to hospital while awaiting delivery. GWG was categorized by using 2 different approaches. In the first approach, GWG was categorized in quartiles according to different pre-pregnancy BMI groups. In the second approach, GWG was classified as inadequate, adequate, and excessive according to the 2009 IOM guidelines.

2.3. Measurement of OL

Maternal perception of the onset of lactation is considered a valid public health indicator of OL and had been widely used in other studies [5,6,11,19,20]. On the day 4 postpartum visit, participants were asked to describe the first time they felt their breasts were noticeably fuller than they were before giving birth. We repeated these interview questions on day 5 if the women did not feel their breasts fuller in the previous visit, and subsequently by means of telephone interviews. Delayed OL was defined as maternal perception of onset of noticeable fullness after 72 h postpartum.

2.4. Covariates

Covariates information obtained from a structured questionnaire at enrollment including maternal age when enrolled (year), ethnicity (Han Chinese/others), education level, average personal income (per month, Chinese Yuan), smoking (active smoking or smoking before pregnancy, defined as ≥3 times a week, yes/no, respectively), alcohol consumption (active drinking or drinking before pregnancy, defined as ≥3 times a week, yes/no, respectively), last date of menstrual period (LMP), and parity (primiparous/multiparous).

All the participants received a 75 g, 2-h oral glucose tolerance test (OGTT) during 24–28 weeks of gestation. GDM was diagnosed according to the International Association of the Diabetes and Pregnancy Study Groups recommendation [21]. These guidelines at least consider one value of plasma glucose (PG) concentration to be equal or exceed the threshold of fasting PG of 5.1 mmol/L, 1-h PG of 10.0 mmol/L, and 2-h PG of 8.5 mmol/L.

Information on delivery and neonatal outcomes were obtained from hospital medical records. These included date of birth, delivery mode, neonatal sex, birth weight and length. The number of weeks between birth and the LMP was used to calculate gestational age at delivery.

Information on in-hospital breastfeeding for each mother-infant dyad was obtained by using a LATCH breastfeeding assessment tool [22,23] at day 1 postpartum face-to-face interviews. Each letter in the acronym defined a different area of assessment. “L” describes the ability of the infant to latch onto the breast. “A” describes audible swallowing noted at the breast. “T” describes the type of nipples. “C” describes the comfort level of the mother regarding her breast. “H” measures the amount of help the mother require to position her baby at the breast, each worth 0 to 2 points (0 = did not exhibit target behavior, 2 = readily exhibited target behavior) for a possible total score of 10. We divided LATCH scores as ≤8 vs > 8, with lower scores indicating suboptimal breastfeeding.

2.5. Statistical analysis

Descriptive statistics were presented as percentages for categorical variables and means ± SDs for continuous variables. To test for differences of demographic characteristics of pregnant women among different OL status, continuous variables were compared using one-way analysis of variance (ANOVA), and the χ^2 test was used for categorical variables. Binary logistical regression analysis was used to assess the association between pre-pregnancy BMI, GWG and delayed OL, and the Results were presented as odds ratios (ORs) with 95% confidence intervals (CIs).

In the pre-pregnancy BMI analysis, women of normal weight were used as the reference group and those with BMI ≥24 kg/m^2 were grouped together because only 1.4% (47/3282) of the women were ≥28 kg/m^2. For the GWG analysis, GWG was categorized in quartiles according to the pre-pregnancy BMI status, and the lowest quartile was used as reference group. *P*-values for linear trend were calculated by entering the median value of each category of GWG as a continuous variable in the models. GWG was also classified as inadequate, adequate, or excessive by using the 2009 IOM guidelines, and adequate is used as the reference group. Based on previous literature and directed acyclic graphs, covariates included in adjusted model were: maternal age, parity, GDM, pre-pregnancy BMI, gestational age at birth, neonatal birth weight, and breastfeeding information evaluated by LATCH score at day 1 postpartum.

Effect estimates were not adjusted for delivery mode because it may mediate the association between GWG and delayed OL. Postpartum BMI was also not adjusted in models due to the strong correlation with GWG ($r = 1$, $P < 0.001$, data not shown). Neonatal birth weight and LATCH-score are often strong predictors of delayed OL and were therefore considered as potential confounders. However, we recognize that these variables could lie on the causal pathway between GWG and OL. Therefore, we calculated the risk in different models. Mode I was adjusted for maternal age, parity, GDM, and gestational age at birth. Model II included additional adjustment for neonatal birth weight and LATCH-score. We used multiple imputation, based on 5 replications, to fill in missing values of education, income and LATCH-score. And the Results of pooled analyses are presented. To evaluate whether the imputation of missing data have affected the results, we also performed sensitivity analyses on participants with complete data ($n = 3065$). We also performed additional sensitivity analyses to assess the robustness of the results. To reduce error due to self-reported pre-pregnancy weight at the enrollment, we analyzed GWG from the initial prenatal visit to the LAWM.

All data were analyzed using Empower Stats software, version 2.14.9 (X&Y Solutions Inc. Boston, MA) and R software (The R Project for Statistical Computing, version 3.3.1), and $P < 0.05$ was considered to be statistically significant.

3. Results

3.1. Subject characteristics

A total of 3282 eligible women from TMCHC study were included for final analysis. The average age of the participants was 28.3 ± 3.4 years old and pre-pregnancy BMI was 20.8 ± 2.6 kg/m^2, 18.4% (604/3282) were identified as delayed OL. Table 1 summarizes the demographic, anthropometric, labor and delivery, newborn, and breastfeeding characteristics of the participants based on lactogenesis status. Women developed delayed OL were more likely to be primiparous, have a larger baby, and have higher BMI after delivery compared with women developed timely OL. The LATCH-score was also lower among women who developed delayed OL. There were no significant differences in age at enrollment, education level, income, smoking, alcohol consumption, delivery mode, and fetal sex.

Table 2 presents distribution of GWG levels based on pre-pregnancy BMI category. 2296 (69.9%) were normal weight, 619 (18.9%) were underweight, and 367 (11.2%) were overweight or obese. The average GWG for the normal weight women was 16.1 ± 4.5 kg, more details are shown in Table 2.

3.2. Pre-pregnancy BMI, GWG and delayed OL

Table 3 presents logistic regression Results for delayed OL associated with the pre-pregnancy BMI and GWG. In the pre-pregnancy BMI analysis, the adjusted ORs (95% CIs) were 0.83 (0.66, 1.06) for underweight and 0.81 (0.60, 1.09) for overweight, when compared with the normal weight group. When GWG categorized in quartiles according to their pre-pregnancy BMI status, odds of delayed OL in the third and fourth versus the lowest quartile of GWG were 1.48 (1.14, 1.94) and 1.46 (1.11, 1.90), respectively after adjusting for demographic and maternal prenatal information. When further adjusting for neonatal birth weight and LATCH-score in model II, the association remained significant (1.47 [95% CI: 1.13, 1.92], 1.42 [95% CI: 1.08, 1.86]; P for trend = 0.006). When GWG was classified into 3 groups according to the 2009 IOM guidelines, compared with women with adequate GWG, the adjusted ORs (95% CIs) were 0.82 (95% CI: 0.61, 1.10) for inadequate GWG and 1.13 (95% CI: 0.93, 1.38) for excessive GWG. Two sensitivity analyses were conducted to assess the robustness of the results. First, we excluded participants with incomplete data and found the results remained highly similar (Table S1). Second, we calculated GWG by weight measured from the initial prenatal visit to the LAWM and also found that higher GWG quartiles remained significantly associated with elevated risk of delayed OL in adjusted models. Compared with those in the lowest quartile, the ORs (95% CIs) were 1.32 (1.00, 1.56) for quartile 2, 1.35 (1.02, 1.78) for quartile 3, and 1.65 (1.25, 2.18) for quartile 4 (Table S2).

4. Discussion

This prospective cohort study, to our knowledge, provides the largest observational study so far to examine the association between GWG and the risk of delayed OL. Our analysis showed that 18.4% of mothers in this population experienced delayed OL when the maternal perception of breast fullness was used as lactogenesis cue. And we found that higher GWG was significantly associated with a greater risk of delayed OL.

The 18.4% incidence of delayed OL reported in our study is lower than that observed in the United States and Australia (22%–44%) [5,6,11,19,24], but higher than that reported for women in Guatemala (10%) [7] and the Anhui Province of China (9.8%) [25]. This variation in the incidences of delayed OL between countries may point to differences in study design, maternal characteristics, as well as, types of hospital and cultural practices.

In our study, when GWG was categorized in quartiles, women who were in higher 2 quartiles were more likely to have delayed OL compared with those in the lowest quartile, while no association between GWG and delayed OL was observed when GWG was classified according to 2009 IOM guidelines. Similarly, a study conducted in California suggested that delayed OL occurred more frequently among women who gained weight >14 kg than ≤14 kg [6]. In our study, the cutoff value was 16 kg for normal weight and 15 kg for overweight women. A study based on the IFPS II cohort found that excessive GWG was associated with delayed OL among non-Hispanic white women but not in other racial/ethnic groups, when GWG was classified according to the 2009 IOM guidelines [16]. This indicated that the GWG guidelines recommended by IOM may not be applicable to all populations.

Contrary to the Results of most previous studies, where a positive association of pre-pregnancy overweight with delayed OL was identified [9–12,19], we observed no such association. The inconsistence may be due to the different characteristics in study populations. Compare to the mean pre-pregnancy BMI of 28.7 ± 6.2, 29.3 ± 7.0, and 31.3 ± 7.9 kg/m^2 respectively in previous studies [11,12,19], the participants' pre-pregnancy BMI in our study was 20.8 ± 2.6 kg/m^2 and only 11.2% of them were overweight or obese, which is much lower than that of those studies (34.9%, 70.1%, 68.5%)) from European populations. This may partially explain why our study failed to detect potential association between overweight or obesity and delayed OL. More researches with large sample sizes of overweight and obese women are required to determine whether or not these association exist in Asian population.

The mechanism underlying the association of higher GWG and increased risk of delayed OL may due to the effect of maternal obesity. Animal studies have observed that obesity led to impaired lactation performance [26]. In humans, the immediately drop in progesterone concentration postpartum is considered as the trigger for OL and maintenance of prolactin also contributes to the process [2]. An earlier study indicated that mothers with obesity showed lower prolactin response to an infant sucking [14]. Thus, this lower prolactin lead to restrained trigger for OL, and resulted in increased risk of delayed OL. What's more, insulin may be another possible

Table 1
Maternal, labor and delivery, newborn, breastfeeding characteristics in women by lactogenesis status (n = 3282)[a].

Variables	Overall	Delayed OL		P^b
		No	Yes	
N	3282	2678	604	–
1) Maternal prenatal characteristics				
Age (y)	28.3 ± 3.4[2]	28.4 ± 3.4	28.1 ± 3.1	0.120
Gestational age at enrolment (wk)	12.8 ± 1.8	12.8 ± 1.8	12.8 ± 1.9	0.472
Height (cm)	160.4 ± 5.0	160.5 ± 5.0	160.1 ± 4.7	0.091
Pre-pregnancy weight (kg)	53.5 ± 7.4	53.4 ± 7.4	53.6 ± 7.4	0.720
Pre-pregnancy BMI (kg/m^2)	20.8 ± 2.6	20.7 ± 2.6	20.9 ± 2.5	0.245
Weight at enrollment (kg)	54.7 ± 7.8	54.6 ± 7.8	54.8 ± 7.7	0.715
Weight gain of first trimester (kg)[c]	1.2 ± 2.5	1.2 ± 2.5	1.2 ± 2.7	0.855
Ethnicity (Han Chinese)	3200 (97.5)	2612 (97.5)	588 (97.4)	0.793
Education level (y)				0.325
≤12	349 (10.6)	293 (10.9)	56 (9.3)	
12–15	855 (26.1)	708 (26.4)	147 (24.3)	
≥15	1986 (60.5)	1601 (59.8)	385 (63.7)	
Missing	92 (2.8)	76 (2.8)	16 (2.6)	
Mean household income (¥[d])				0.555
<5000	1178 (35.9)	960 (35.8)	218 (36.1)	
5000–9999	1389 (42.3)	1145 (42.8)	244 (40.4)	
≥10000	668 (20.4)	537 (20.1)	131 (21.7)	
Missing	47 (1.4)	36 (1.3)	11 (1.8)	
Current smoking at enrollment (Yes)	107 (3.3)	83 (3.1)	24 (4.0)	0.402
Alcohol consumption (Yes)	48 (1.5)	35 (1.3)	13 (2.2)	0.118
Parity (Primiparous)	2751 (83.8)	2207 (82.4)	544 (90.1)	<0.001
GDM (Yes)	310 (9.4)	239 (9.2)	71 (11.7)	0.032
2) Labor and delivery				
Delivery mode (Vaginal)	1948 (59.4)	1599 (59.7)	349 (57.8)	0.321
3) Newborn characteristics				
Gestational age at delivery (wk)	39.4 ± 1.1	39.4 ± 1.1	39.5 ± 1.0	0.034
Birth weight (g)				0.011
<2500	23 (0.7)	20 (0.7)	3 (0.5)	
2500–3999	3029 (92.3)	2487 (92.9)	542 (89.7)	
≥4000	230 (7.0)	171 (6.4)	59 (9.8)	
Sex (Male)	1761 (53.7)	1441(53.8)	320 (53.0)	0.712
4) Early breastfeeding				
LATCH-score categories on day 1[e]				<0.001
≤8	1147 (34.9)	900 (33.6)	247 (40.9)	
>8	2054 (62.6)	1712 (63.9)	342 (56.6)	
Missing	81 (2.5)	66 (2.5)	15 (2.5)	
5) Postpartum status at day 4				
Postpartum BMI (kg/m^2)	24.6 ± 2.9	24.6 ± 3.0	24.9 ± 2.8	0.015

Delayed OL, delayed onset of lactogenesis; GDM, gestational diabetes mellitus.
[a] Continuous variables were presented as mean ± SD; categorical variables were showed as percentages (%).
[b] *P* values calculated using $\chi 2$ test for variables of proportion and one-way analysis of variance for continuous variables.
[c] Weight gain of first trimester was calculated as the difference between the weight at enrollment and the pre-pregnancy weight.
[d] ¥, Chinese Yuan; ¥1 ≈ US $ 0.16.
[e] Cutoff was the median value.

Table 2
GWG levels (kg) based on the pre-pregnancy BMI category (n = 3282).

Pre-pregnancy BMI	N (%)	25th	median	75th	mean ± SD
Underweight (<18.5 kg/m^2)	619 (18.9)	13.5	16.0	18.7	16.3 ± 4.0
Normal weight (18.5–23.9 kg/m^2)	2296 (69.9)	13.0	16.0	19.0	16.1 ± 4.5
Overweight (≥24.0 kg/m^2)	367 (11.2)	10.8	15.0	18.2	14.9 ± 5.5

biological mechanism connecting higher GWG with delayed OL. In a vitro research, it showed that insulin stimulated the expression of genes directly involved in milk protein synthesis [27]. Since insulin resistance in obese mothers may restrain milk biosynthesis [28,29], higher GWG may have a negative impact on timely OL. Further studies assessing the association between prolactin and insulin in pregnant women with higher GWG and delayed OL are necessary in the future.

A strength of the current study is the prospective cohort study design. The prospective cohort study design allows us to obtain abundant and accurate covariates, which may avoid confounding bias. And we had a large sample size of 3282 which provided us with a definitive confidence level to examine high GWG with delayed OL. Besides, we categorized GWG not only into 3 groups according to 2009 IOM guidelines, but into 4 groups in quartiles to explore the association of GWG on delayed OL.

With regards to any observational report, our study has several limitations. First, we determined the timing of OL based on maternal perception, which arguably is a subjective assessment. However, this indicator has been shown to strongly correlate with milk transfer [3,6] and biochemical measurements [30]. Delayed OL is an early postpartum outcome; we assessed within 4 days postpartum, which would attenuate recall bias. Second, using self-reported pre-pregnancy weight introduce bias into GWG measurements, but it appears to be a small difference [31]. And self-report is a cost-effective and practical measurement approach

Table 3
Association of delayed OL with pre-pregnancy BMI and GWG from logistic regression (n = 3282).

Variables	Delayed OL/Total	Crude		Model I[a]		Model II[b]	
		OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Prepregnancy BMI[c]							
Normal weight	441/2296	1.00 (1.00,1.00)	1.000	1.00 (1.00,1.00)	1.000	1.00 (1.00,1.00)	1.000
Underweight	101/619	0.82 (0.65, 1.04)	0.101	0.81 (0.64, 1.03)	0.085	0.83 (0.66, 1.06)	0.138
Overweight	62/367	0.86 (0.64, 1.15)	0.294	0.87 (0.65, 1.17)	0.368	0.81 (0.60, 1.09)	0.155
GWG in quartiles							
Quartile 1	113/759	1.00 (1.00,1.00)	1.000	1.00 (1.00,1.00)	1.000	1.00 (1.00,1.00)	1.000
Quartile 2	147/851	1.19 (0.91, 1.56)	0.194	1.20 (0.92, 1.57)	0.187	1.20 (0.91, 1.57)	0.193
Quartile 3	170/826	1.48 (1.14, 1.92)	0.003	1.48 (1.14, 1.94)	0.004	1.47 (1.13, 1.92)	0.005
Quartile 4	174/846	1.48 (1.14, 1.92)	0.003	1.46 (1.11, 1.90)	0.006	1.42 (1.08, 1.86)	0.012
P for trend			0.001		0.003		0.006
GWG of IOM							
Adequate	231/1316	1.00 (1.00,1.00)	1.000	1.00 (1.00,1.00)	1.000	1.00 (1.00,1.00)	1.000
Inadequate	68/456	0.82 (0.61, 1.10)	0.195	0.83 (0.62, 1.12)	0.216	0.82 (0.61, 1.10)	0.181
Excessive	305/1510	1.19 (0.98, 1.44)	0.074	1.17 (0.96, 1.42)	0.111	1.13 (0.93, 1.38)	0.207

Cut-off values for quartiles of GWG levels were <13.5, 13.5–15.9, 16.0–18.6, ≥18.7 kg for underweight; <13.0, 13.0–15.9, 16.0–18.9, ≥19.0 kg for normal; and <10.8, 10.8–14.9, 15.0–18.1, ≥18.2 kg for overweight; Cut-off values for GWG by the 2009 IOM guidelines were <12.5, 12.5–18, >18 kg for underweight; <11.5, 11.5–16, >16 kg for normal weight; and <7, 7–11.5, >11.5 kg for overweight.
Delayed OL, delayed onset of lactogenesis; GWG, gestational weight gain.
[a] Model I was adjusted for maternal age, parity (primiparous, multiparous), GDM (yes, no), and gestational age.
[b] Model II was adjusted as for model 1 and for birth weight (<2500 g, 2500–3999 g, ≥4000 g) and LATCH-score (≤8, >8).
[c] In the pre-pregnancy BMI analysis, GWG as a continuous variable was adjusted additionally.

[32]. With the use of weight gain from the weight measured in initial visit to the LAWM in hospital in a sensitive analysis, we estimated similar Results. Third, GWG is calculated by subtracting pre-pregnancy weight from the LAWM, which is clearly correlated with gestational age at delivery. This approach may produce bias in studies of outcomes that are also associated with gestational duration [33]. However, a previous comparison of observed and predicted measures of GWG (a mixed-effects model to predict GWG over a standardized length of gestation of 39 wk) have shown that they were highly correlated ($r = 0.92$, $P = 0.001$) in a study of term pregnancies [34]. With our study design of term pregnancies, we anticipated that this error would not have produced a bias in estimating associations between GWG and delayed OL. Finally, although we adjusted for various covariates that were associated with delayed OL, other potential variables such as maternal postpartum edema, dietary intake, sleep and activities may be further explored.

5. Conclusions

The present prospective cohort study observed an adverse impact of higher GWG during pregnancy on timely OL. Women who gained too much weight during pregnancy have higher risk of delayed OL and maintaining an optimal gestational weight gain is of significant importance for timely OL. These findings have public health implications and indicate the need for protecting pregnant women from gaining too much weight. Given the study population was almost Han Chinese, future studies conducted among other populations are warranted to confirm our findings.

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Statement of authorship

NY contributed to the conception and designed research; XY, LHao, GS and NY supervised the study conduct; CZ, QL, HY, MX, YZ, XC, XL and LH conducted research; LH and WW analyzed data; LH and XC drafted the manuscript.

Conflict of interest

The authors declared no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.clnu.2018.11.001.

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