Heliyon 10 (2024) e35628

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

The association between maternal fruit consumption before and during pregnancy and fetal growth: The Lanzhou birth cohort study

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ARTICLE INFO

Keywords:
Fruits
Low birth weight
Small for gestational age
Fetal growth
Body mass index

ABSTRACT

Background: The association between maternal fruit consumption and fetal growth remains inconsistent. The current study aimed to determine whether maternal fruit consumption was associated with low birth weight (LBW) or small for gestational age (SGA) babies.

Methods: A large birth cohort study was conducted in Lanzhou, China, from 2010 to 2012 and included 10,076 pregnant women at the 1st, 2nd, and 3rd trimester of pregnancy for analysis. Fruit consumption in the 1st, 2nd, and 3rd trimester of pregnancy was measured by a self-designed food frequency questionnaire (FFQ) and divided into three groups: 1) inadequate fruit consumption: <200 g/d for the1st, 2nd, and 3rd trimester; 2) adequate fruit consumption: 200–350 g/d for the 1st trimester or 200–400 g/d for the 2nd and 3rd trimester; 3) excessive fruit consumption: >350 g/d for the 1st trimester or > 400 g/d for the 2nd and 3rd trimester. A case-control study was used to analyze the association between fruit intake during pregnancy and low birth weight infants.

Results: Compared to adequate fruit consumption, excessive fruit consumption throughout each trimester of pregnancy was associated with a lower risk of LBW, with an odds ratio (OR) ranging from 0.70 to 0.79 (95 % confidence interval, CI: 0.57–0.98); while inadequate fruit consumption was associated with a higher risk of infant LBW, with an OR ranging from 1.26 to 1.36 (95%CI: 1.04–1.66). After stratifying by mother's pre-pregnancy body mass index (BMI), the results were similar among women with underweight BMI. No significance was found between fruit consumption and SGA in the general population. Still, stratified analyses showed that inadequate fruit consumption was associated with an increased risk of SGA in underweight mothers, with an OR ranging from 1.66 to 1.79 (95%CI: 1.13–2.64).

Conclusions: Fruit consumption during pregnancy reduces the risk of LBW in Chinese women, especially in women with low pre-pregnancy BMI.

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https://doi.org/10.1016/j.heliyon.2024.e35628
Received 30 January 2024; Received in revised form 30 July 2024; Accepted 1 August 2024
Available online 5 August 2024
2405-8440/

1. Introduction

Abnormal infant birth weight is a leading cause of infant mortality and morbidity [1,2]. Low birth weight (LBW), has been defined by World Health Organization (WHO) as weight at birth of <2500 g (5.5 pounds)., is a major public health concern and contributes to 80 % of neonatal deaths worldwide [3]. The global prevalence of LBW is estimated to be 14.6 % (20.5 million), with 91 % concentrated in low-and-middle-income countries [4]. Small for gestational age (SGA) is defined by the WHO as a birth weight below the 10th percentile by sex for the gestational age [5]. SGA has been shown to increase the risk for developmental delay and behavioral problems including inattention and aggressive behaviors even in full-term infants [6,7]. Both LBW and SGA are associated with a higher risk of mortality and morbidity in the neonatal period [8,9].

Consumption of fruits during pregnancy is universally promoted as part of a nutrient-dense diet to prevent abnormal fetal growth [10,11]. Fruits are key sources of essential nutrients such as vitamins, potassium, magnesium, folate, and dietary fiber [12]. In addition, fruits are rich in other bioactive substances, such as phytochemicals, which can provide ideal health benefits beyond essential nutrition and reduce the risk of major chronic diseases [13]. As a result, fruit consumption has been highly recommended for pregnant women. For instance, the American Dietary Guidelines suggest that at least one-half plate of fruits and vegetables should be consumed each meal for the general population [14]. The Chinese Journal of Perinatal Medicine Dietary Guidelines recommends pregnant women have a daily intake of 200–400 g of fresh fruit during the second and last trimester [15]. Several national authorities in other countries even recommend eating up to 650 g of fruit and vegetables daily [16].

The association between maternal fruit consumption and fetal growth remains unclear and inconsistent. A systematic review by Murphy et al. found limited inconclusive evidence on the protective role of increased fruit consumption on infant birth weight [17]. On the other hand, no significant association between fruit consumption and birth weight was found in the studies by Petridou et al. [18], Mikkelsen et al. [19], and Ramon et al. [20].In addition, Mitchell et al. [21], Ramon et al. [20], McCowan et al. [22], and Ricci et al. [23] found that fruit consumption was also not significantly associated with the risk of SGA after adjusting other confounders. However, several studies also showed a significant association between fruit consumption and fetal growth. For instance, Martínez-Galiano et al.'s study showed a negative association between fruit consumption of >420 g/day with SGA [11]. Rao et al.'s study showed that increased maternal fruit consumption was associated with increased birth size after adjusting for other confounders [24]. A Danish National Birth Cohort study also reported that fruit consumption in pregnancy was positively associated with higher birth weight in infants, especially among underweight pregnant women [19].

The inconsistent conclusions in the association between maternal fruit consumption and fetal growth may be explained by variability across the studies, such as study location, study periods, the assessment of exposure and outcome variables, and the adjustment of confounders. Since most previous studies were conducted in Western countries, much less is known about maternal fruit consumption and fetal growth in China. The current study was conducted to determine whether maternal fruit consumption before and

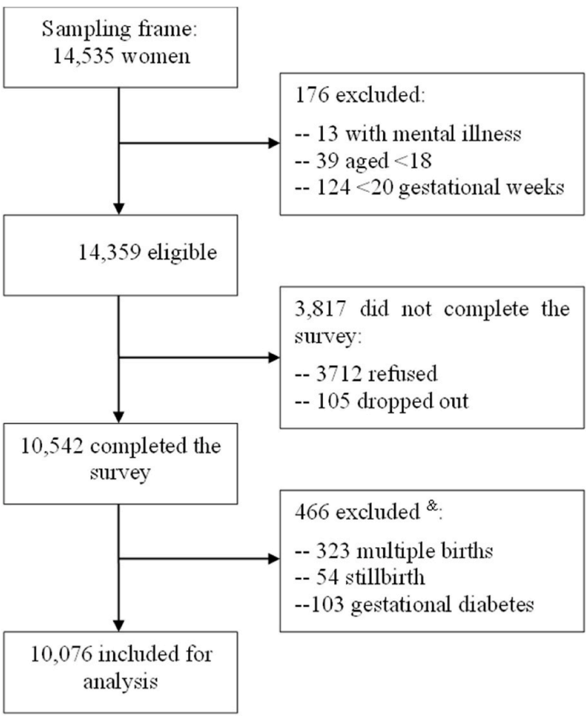

Fig. 1. Flow chart of participant enrolment and inclusion for analysis. Note: & the number of each type does not add up to 466 due to comorbidity of gestational diabetes, multiple births, and stillbirth (n = 14).

during pregnancy was associated with infant LBW or SGA in a large birth cohort in Lanzhou, China. Specifically, we examined such an association in three time periods: 1st, 2nd, and 3rd trimesters of pregnancy. Additionally, due to the increasing trend of pre-pregnancy underweight among women of childbearing age in China, we conducted stratified analysis on the association between maternal fruit consumption and infant LBW or SGA based on pre-pregnancy body mass index(BMI) .

2. Materials and methods

2.1. Study population and procedure

Data were collected from pregnant women who participated in the Lanzhou Birth Cohort Study conducted between 2010 and 2012 at the Gansu Provincial Maternity and Child Care Hospital, located in Lanzhou City, Gansu Province, China. The target participants were pregnant women who gave birth at ≥ 20 gestational weeks, without mental illness, and aged ≥18. Fig. 1 shows the flowchart of participant recruitment and inclusion for analysis. The original sampling frame included all pregnant women who came to the hospital for delivery (n = 14,535), among whom 176 were excluded due to delivery at < 20 gestational weeks (n = 124), mental illness (n = 13), and aged <18 (n = 39). Thus, a total of 14,359 pregnant women were deemed eligible for the study and approached for participation, among whom 3817 did not complete the study due to refusal (n = 3712) and dropout during the study (n = 105). Among the 10,542 (73.4 %) pregnant women who completed the questionnaires, 466 were excluded due to multiple births (n = 323), stillbirth (n = 54), and gestational diabetes mellitus (n = 103), including 14 women with comorbidity of gestational diabetes and multiple births/stillbirths. Finally, a total of 10,076 (95.6 %) women with a singleton live birth were included in the final analysis. Detailed information on the Lanzhou Birth Cohort has been published elsewhere [25,26].

All study procedures were approved by the human investigation committees at the Gansu Provincial Maternity and Child Care Hospital and Yale University. Eligible women were included in the study at their first prenatal examination visits to the hospital. After obtaining written consent, trained research interviewers conducted face-to-face interviews with a standardized and structured questionnaire. Information of birth outcomes and pregnancy complications were abstracted from the medical records; birth weight was measured right after birth; gestational age was adjusted for the mother's last menstrual period (LMP) combined with an ultrasound; an early ultrasound of the crown-rump length was used when the LMP differences exceed 7 days.

2.2. Exposure variables

A self-designed food frequency questionnaire (FFQ) was used to collect information on fruit consumption during three time periods: 1st, 2nd, and 3rd trimester of pregnancy. The FFQ was designed explicitly for the Lanzhou Birth Cohort Study and developed by nutritional experts from the U.S. and China based on expert consultation, group discussion, and a literature review of past validated questionnaires. Although the FFQ has not been validated in other studies, it was scientifically developed and satisfied the requirements for nutritional studies. The full FFQ was in line with the standards of nutrition research and collected information on 34 categories of food consumption, including fruit, rice, seafood, vegetables, meat, dairy, *etc*. The FFQ was administered at 13 gestational weeks to assess food consumption in the 1st trimester of pregnancy (from conception to 12 weeks), at 27 gestational weeks to assess food consumption in the 2nd trimester of pregnancy (12–24 weeks), and within 3 days post-delivery to assess food consumption in the 3rd trimester of pregnancy (24–40 weeks). For the purpose of this study, we only extracted two items on fruit consumption from the FFQ that inquired about whether the participants consumed any fruit, and, on average, how much fruit the participants consumed each day. According to the recommendation from the Chinese Journal of Perinatal Medicine Dietary Guidelines [15,27],we divided the fruit consumption frequency into three groups: inadequate, adequate, and excessive fruit consumption. Previous research and guidelines suggest that nutritional requirements differ by different pregnancy stages, and pregnant women have a lower demand for energy and nutrients in early pregnancy due to relatively slower fetal growth [15,28]. Therefore, we used different cutoffs for fruit consumption by different trimesters. The classification criteria for pre-pregnancy and early pregnancy are: 1) inadequate fruit consumption: <200 g/d; 2) adequate fruit consumption: 200–350 g/d; 3) excessive fruit consumption: >350 g/d; the classification criteria for the 2nd and 3rd trimesters of pregnancy are: 1) inadequate fruit consumption: <200 g/d; 2) adequate fruit consumption: 200–400 g/d; 3) excessive fruit consumption: >400 g/d.

2.3. Outcome variables

LBW and SGA were used as outcome variables. Information concerning birth weight (g) was obtained from birth records. Low birth weight has been defined by WHO as weight at birth of <2500 g (5.5 pounds). NBW, defined as birth weight ≥2500 g and < 4000 g [29]. Fetal weight percentiles for births were calculated using the FETALGPSXL tool (a simple spreadsheet-based calculator) with the Intergrowth 21st standard [1,2]. According to the percentile of birth weight for gestational age, newborns were categorized into three groups: SGA (<10th percentile), appropriate for gestational age (AGA) (10th-90th percentile; reference group), and large for gestational age (LGA) (>90th percentile) [5].

2.4. Confounders

Confounders that may affect both the exposure and outcome variables were measured based on previous studies [17]. These confounders included socio-demographical characteristics (such as age, education, and income), health behaviors and lifestyles (such as pre-pregnancy BMI, whether attend pregnancy health care, first perinatal examination, smoking, and drinking), birth outcomes (such as natural pregnancy, ways of delivery, baby gender, gestational weight gain (GWG), and pregnancy complications (such as vaginal hemorrhage, preeclampsia, and postpartum hemorrhage). Postpartum hemorrhage was defined as more than 500 mL of blood loss in vaginal delivery within 24 h of delivery or more than 1000 mL of blood loss in cesarean delivery [30]. Preeclampsia was defined as maternal systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg measured on two occasions at least 4 h apart, and proteinuria ≥0.3 g on a 24-h urinary collection or a protein (mg/dL)/creatinine (mg/dL) ratio ≥0.3, or a urine dipstick

Table 1
Comparison of maternal characteristics between LBW and NBW groups in the 2010–2012 Lanzhou Birth Cohort Study (n = 10, 076).

Variable	NBW (n, (%))	LBW	
		n (%)	*P*
Whether attend pregnancy health care			
No	4121 (48.9)	531 (64.4)	<0.0001
Yes	4308 (51.1)	293 (35.6)	
First perinatal examination time			
1st trimester	5568 (67.0)	583 (72.1)	0.0002
2nd trimester	2644 (31.2)	209 (25.8)	
3rd trimester	93 (1.1)	17 (2.1)	
Age			
< 25 y	1340 (15.7)	208 (24.6)	<0.0001
25-34	6440 (75.5)	519 (61.4)	
≥ 35	755 (8.9)	118 (14.0)	
Education level			
≤ 9 y	1770 (21.1)	347 (42.2)	<0.0001
10-12	1451 (17.3)	165 (20.1)	
≥ 13	5164 (61.5)	310 (37.7)	
Family's average monthly income			
< 3000	4220 (54.6)	554 (72.8)	<0.0001
3000	3503 (45.4)	207 (27.2)	
Vaginal hemorrhage			
No	5467 (82.8)	672 (72.5)	<0.0001
Yes	1139 (17.2)	173 (27.5)	
Natural pregnancy			
No	279 (4.4)	27 (4.4)	0.9996
Yes	6065 (95.6)	587 (95.6)	
Postpartum hemorrhage			
No	8299 (97.2)	800 (94.7)	<0.0001
Yes	236 (2.8)	45 (5.3)	
Active smoke			
No	8466 (99.2)	836 (98.9)	0.4332
Yes	69 (0.8)	9 (1.1)	
Passive smoke			
No	6916 (81.0)	641 (75.9)	0.0003
Yes	1619 (19.0)	204 (24.1)	
Alcohol use			
No	8518 (99.8)	842 (99.6)	0.3488
Yes	17 (0.2)	3 (0.4)	
Primipara			
Yes	6281 (73.6)	511 (60.5)	<0.0001
No	2254 (26.4)	334 (39.5)	
Baby gender			
Male	4425 (51.9)	417 (49.5)	0.1699
Female	4094 (48.1)	426 (50.5)	
Ways of delivery			
Vaginal	5468 (64.5)	395 (49.0)	<0.0001
Cesarean	3016 (35.6)	412 (51.1)	
Mother's BMI (kg/m^2)	20.6 ± 2.65	20.8 ± 3.05	0.0530
Underweight	1810 (21.9)	182 (23.0)	0.0566
Normal weight	5626 (68.1)	511 (64.6)	
Overweight	826 (10.0)	98 (12.4)	
Preeclampsia			
No	8216 (97.9)	682 (85.3)	<0.0001
Yes	174 (2.1)	118 (14.8)	
Gestational Weight Gain (GWG)			
I-GWG	971 (11.8)	271 (35.5)	<0.0001
A-GWG	2838 (34.6)	257 (33.7)	
E-GWG	4397 (53.6)	235 (30.8)	

Note: NBW: normal birth weight; LBW: low birth weight; I-GWG: inadequate gestational weight gain; A-GWG: adequate gestational weight gain; E-GWG: excessive gestational weight gain.

protein of 1+, after 20 weeks of gestation [31]. GWG was calculated as the difference between the weight prior to pregnancy and prior to delivery [32] and was classified into the following three categories: inadequate GWG (I-GWG), adequate GWG (A-GWG), and excessive GWG (E-GWG) [33]. Pregnancy health care refers to the process of assessing the risk factors for adverse pregnancy outcomes in men and women of childbearing age from the aspects of physical, psychological, and social behavior and then adopting preventive and intervention measures to maintain and promote the health status of both parties [34]. BMI was calculated by body weight as measured in kilograms divided by the square of height measured in meters (kg/m^2) [35]. The Chinese BMI classification was based on

Table 2
Comparison of maternal characteristics between SGA and AGA groups in the 2010–2012 Lanzhou Birth Cohort Study (n = 10, 076).

Variables	AGA (n (%))	SGA	
		n (%)	*P*
Whether attend pregnancy health care			
No	3862 (49.7)	455 (59.2)	<0.0001
Yes	3910 (50.3)	313 (40.8)	
First perinatal examination time			
1st trimester	5135 (67.1)	534 (71.0)	0.0025
2nd trimester	2434 (31.8)	202 (26.9)	
3rd trimester	89 (1.2)	16 (2.1)	
Age			
< 25 y	1285 (16.3)	170 (21.7)	<0.0001
26–34 y	5880 (74.7)	529 (67.6)	
≥ 35 y	711 (9.0)	84 (10.7)	
Education level			
9	1684 (21.8)	278 (36.3)	<0.0001
10-12	1345 (17.4)	144 (18.8)	
13	4701 (60.8)	345 (45.0)	
Family's average monthly income			
< 3000	3952 (55.4)	474 (67.80)	<0.0001
3000	3187 (44.6)	225 (32.2)	
Vaginal hemorrhage			
No	4984 (82.0)	479 (79.7)	<0.1608
Yes	1093 (18.0)	122 (20.3)	
Natural pregnancy			
No	260 (4.5)	30 (5.2)	0.3948
Yes	5589 (95.6)	545 (94.8)	
Postpartum hemorrhage			
No	7656 (97.2)	754 (96.3)	0.1460
Yes	220 (2.8)	29 (3.7)	
Active smoke			
No	7809 (99.2)	774 (98.9)	0.3927
Yes	67 (0.9)	9 (1.2)	
Passive smoke			
No	6381 (81.0)	591 (75.5)	0.0002
Yes	1495 (19.0)	192 (24.5)	
Alcohol use			
No	7860 (99.8)	781 (99.7)	0.7594
Yes	16 (0.2)	2 (0.3)	
Primipara			
No	5754 (73.1)	536 (68.5)	<0.0059
Yes	2122 (26.9)	247 (31.6)	
Baby gender			
Male	4132 (52.6)	387 (49.5)	0.1006
Female	3726 (47.4)	395 (50.5)	
Ways of delivery			
Vaginal delivery	5044 (64.6)	416 (54.1)	<0.0001
Cesarean section	2767 (35.4)	353 (45.9)	
Mother's BMI			
Underweight	1698 (22.3)	196 (26.4)	0.0137
Normal weight	5191 (68.1)	467 (62.9)	
Overweight	730 (9.6)	79 (10.7)	
Preeclampsia			
No	7558 (97.6)	657 (88.2)	<0.0001
Yes	183 (2.4)	88 (11.8)	
Gestational Weight Gain (GWG)			
I-GWG	1008 (13.3)	182 (25.0)	<0.0001
A-GWG	2650 (35.1)	269 (37.0)	
E-GWG	3897 (51.6)	277 (38.1)	

Note: AGA: appropriate for gestational age; SGA: small for gestational age; I-GWG: inadequate gestational weight gain; A-GWG: adequate gestational weight gain; E-GWG: excessive gestational weight gain; y: years.

the Guidelines for the Prevention and Control of Overweight and Obesity in Adults in China, which defines underweight as BMI <18.5 kg/m^2, normal weight as BMI between 18.5 and 23.9 kg/m^2, overweight as BMI between 24 and 27.9 kg/m^2, and obesity as BMI >28 kg/m^2 [36].In this study, we merged overweight and obesity as one group because of the limited number of cases.

2.5. Statistical analysis

We used the $\chi 2$ test or Fisher's exact test to compare maternal characteristics between LBW and normal birth weight (NBW) groups, and between SGA and AGA groups. The association between fruit consumption and risk of LBW/SGA was analyzed first using unadjusted univariate logistic regression, followed by multivariate logistic regression adjusting for all confounders to calculate Odds ratios (OR) and 95 % confidence intervals (CI). To adjust the total calorie intake of different fruit consumption, we used the statistical model suggested by Willett and Stampfer [37,38]. We took the residual from a linear, least-squares regression model with the total energy intake as the dependent variable and the macronutrient as the independent variable [37,38]. A review has shown that the number of pregnant women with underweight pre-pregnancy BMI has been increasing sharply, which is also the leading cause of infant LBW [39]. Besides, a national prospective cohort study in Danish showed the strongest association between maternal fruit consumption and infant birth weight among women with underweight pre-pregnancy BMI [19]. Based on the previous well-established evidence, we selected pregnant women with underweight pre-pregnancy BMI specifically to explore the association between fruit consumption and LBW and SGA among this group as our subgroup analysis. All statistical analyses were performed using SAS statistical software, version 9.4 (SAS Institute Inc., Cary, NC, USA. TS1M4).

3. Results

3.1. Maternal characteristics and comparisons between LBW and NBW, SGA and AGA

A total of 10,076 women with a singleton live birth were included in the final analysis. Among the 10,076 newborn infants, 845 (8.4 %) were LBW, and 8535 (84.7 %) were NBW, while 783 (7.8 %) were SGA, and 7876 (78.2 %) were AGA. Most participants were between 25 and 34 years old, had a college or above education, and completed their first perinatal examinations during their first pregnancy. More than half attended pregnancy health care and had a family average monthly income of 3000 yuan of Chinese renminbi (RMB) or less per person. Tables 1 and 2 show comparisons of maternal characteristics between LBW and NBW groups and between SGA and AGA groups, which showed significant group differences in most variables. For instance, participants with older age, lower education, and lower family income were more likely to give birth to babies with LBW and SGA.

3.1.1. The association between fruit consumption and risk of LBW

Table 3 shows the association between fruit consumption and LBW by univariate and multivariate analysis. Univariate analysis consistently showed a positive association between increased fruit consumption and decreased risk of LBW in the 1st, 2nd, and 3rd trimesters of pregnancy. Adjusted multivariate logistic regression analysis controlling for all confounders showed a similar significant association between excessive fruit consumption and risk of LBW (OR: 0.72, 95 % confidence interval (CI): 0.50–1.02). Compared to

Table 3
The association between fruit consumption and LBW in the 2010–2012 Lanzhou Birth Cohort Study (n = 10, 076).

Trimester	Amount of fruit intake (g/d)	NBW (n (%))	LBW			
			n (%)	OR (95%CI)	aOR (95%CI)	*P* [a]
Before pregnancy	<200	4565 (57.0)	512 (65.5)	1.33 (1.13–1.57)	1.26 (1.04–1.52)	<0.0001
	200–350	2606 (32.6)	220 (28.1)	Reference	Reference	
	>350	834 (10.4)	50 (6.4)	0.71 (0.52–0.98)	0.72 (0.50–1.02)	
	P for trend	0.0001				
1st	<200	2268 (27.7)	310 (38.8)	1.41 (1.20–1.67)	1.35 (1.12–1.63)	<0.0001
	200–350	3194 (39.1)	309 (48.6)	Reference	Reference	
	>350	2718 (33.2)	181 (22.6)	0.69 (0.57–0.83)	0.70 (0.57–0.86)	
	P for trend	0.0013				
2nd	<200	2123 (25.9)	298 (37.2)	1.50 (1.27–1.77)	1.34 (1.10–1.62)	<0.0001
	200–400	3474 (42.4)	325 (40.6)	Reference	Reference	
	>400	2600 (31.7)	178 (22.2)	0.73 (0.61–0.89)	0.79 (0.64–0.98)	
	P for trend	0.0021				
3rd	<200	2103 (25.7)	290 (37.4)	1.52 (1.28–1.80)	1.36 (1.12–1.66)	<0.0001
	200–400	3469 (42.4)	314 (40.5)	Reference	Reference	
	>400	2604 (31.9)	171 (22.1)	0.73 (0.60–0.88)	0.76 (0.61–0.95)	
	P for trend	0.0144				

Note: NBW: normal birth weight; LBW: low birth weight; OR: odds ratio; aOR: adjusted odds ratio; CI: confidence interval.
[a] adjusted P-values. The following Confounders were controlled for: whether attend pregnancy health care, first perinatal examination, age, education level, family's average monthly income, vaginal hemorrhage, natural pregnancy, postpartum hemorrhage, active smoke, passive smoke, alcohol use, primipara, baby gender, ways of delivery, mother's BMI, and Gestational Weight Gain (GWG)，Preeclampsia, First trimester(1st),Second trimester(2nd),Third trimester(3rd).

adequate fruit consumption, excessive fruit consumption in the 1st, 2nd, and 3rd trimester of pregnancy each was associated with a decreased risk of infant LBW, with OR ranging from 0.70 to 0.79 (95%CI: 0.57–0.98); while inadequate fruit consumption in the 1st, 2nd, and 3rd trimester of pregnancy each was associated with an increased risk of infant LBW, with OR ranging from 1.26 to 1.36 (95% CI: 1.04–1.66). In addition, a significant P for trend was observed in the 1st, 2nd, and 3rd trimester of pregnancy.

3.1.2. The association between fruit consumption and risk of SGA

Table 4 shows the association between fruit consumption and SGA both by univariate analysis and multivariate analysis. Univariate analysis consistently showed positive association between increased fruit consumption with decreased risk of SGA in the 1st, 2nd, and 3rd trimester of pregnancy. However, all those significant associations disappeared in the subsequent adjusted multivariate logistic regression analysis controlling for all confounders, though significant P for trend was observed in the 1st, 2nd, and 3rd trimester of pregnancy.

3.1.3. Stratified analysis of fruit consumption and risk of LBW among underweight mothers

Table 5 shows stratified analyses of the associations between fruit consumption and risk of LBW among mothers with underweight pre-pregnancy BMI. Multivariate logistic regression analyses generally showed a significant inverse relationship between fruit consumption and the risk of LBW among pregnant women with low pre-pregnancy BMI. Compared to the adequate fruit consumption group, the excessive fruit consumption group in the 1st trimester of pregnancy showed a decreased risk of infant LBW (OR: 0.64; 95% CI: 0.41–0.98), while the inadequate fruit consumption group in the 3rd trimester of pregnancy showed an increased risk of infant LBW (OR: 1.49; 95%CI: 1.03–2.17). All other groups showed non-significant differences in infant LBW risk with the reference group, though a significant *P* for trend was observed in the 1st, 2nd, and 3rd trimesters of pregnancy.

3.1.4. Stratified analysis of fruit consumption and risk of SGA among underweight mothers

Table 6 shows stratified analyses of associations between fruit consumption and risk of SGA among mothers with underweight pre-pregnancy BMI. Multivariate logistic regression analyses generally showed an increased risk of SGA with decreased fruit consumption among pregnant women with low pre-pregnancy BMI. Compared to the adequate fruit consumption group, the inadequate fruit consumption group in the 2nd and 3rd trimesters of pregnancy had an increased risk of SGA birth, with OR ranging from 1.66 to 1.79 (95%CI: 1.13–2.64); while the excessive fruit consumption group showed no significant difference in SGA birth risk. In addition, a significant P for trend was observed in the 2nd and 3rd trimesters of pregnancy.

4. Discussion

In the large Lanzhou Birth Cohort Study, we examined the association between maternal fruit consumption in the 1st, 2nd, and 3rd trimesters of pregnancy and the risk of delivering an Low birth weight (LBW) or Small for gestational age (SGA) baby. Our results generally showed an opposite association between fruit consumption and the risk of LBW, but not SGA. Compared to adequate fruit consumption, excessive fruit consumption in the 1st, 2nd, and 3rd trimester of pregnancy was associated with a lower risk of infant LBW. In contrast, inadequate fruit consumption in the 1st, 2nd, and 3rd trimester of pregnancy was associated with a higher risk of

Table 4

The association between fruit Intake consumption and SGA in the 2010–2012 Lanzhou Birth Cohort Study (n = 10, 076).

Trimester	Amount of fruit intake(g/d)	AGA (n (%))	SGA			
			n (%)	OR (95%CI)	aOR (95%CI)	$P^{\#}$
Before pregnancy	<200	4246 (57.5)	438 (60.1)	1.05(0.89–1.24)	1.01(0.84–1.22)	<0.0001
	200–350	2376 (32.2)	234 (32.1)	Reference	Reference	
	>350	758 (10.3)	57 (7.8)0.03	0.76 (0.57–1.03)	0.76 (0.54–1.06)	
	P for trend	0.05				
1st	<200	2139 (28.4)	264 (35.3)	1.24 (1.04–1.48)	1.20 (0.98–1.47)	<0.0001
	200–350	2941 (39.0)	292 (39.0)	Reference	Reference	
	>350	2464 (32.7)	193 (25.8)	0.79 (0.65–0.95)	0.89 (0.72–1.10)	
	P for trend	0.003				
2nd	<200	2010 (26.6)	245 (32.7)	1.20 (1.00–1.42)	1.10 (0.89–1.34)	<0.0001
	200–400	3175 (42.0)	324 (43.2)	Reference	Reference	
	>400	2375 (31.4)	181 (24.1)	0.75 (0.62–0.90)	0.88 (0.72–1.10)	
	P for trend	0.010				
3rd	<200	1986 (26.4)	249 (33.4)	1.27 (1.07–1.52)	1.18 (0.98–1.45)	<0.0001
	200–400	3172 (42.2)	313 (42.0)	Reference	Reference	
	>400	2365 (31.4)	183 (24.6)	0.78 (0.65–0.95)	0.90 (0.73–1.11)	
	P for trend	0.0144				

Note: AGA: appropriate for gestational age; SGA: small for gestational age; OR: odds ratio; aOR: adjusted odds ratio; CI: confidence interval. # adjusted P-values. The following confounders were controlled: whether attend pregnancy health care, first perinatal examination, age, education level, family's average monthly income, vaginal hemorrhage, natural pregnancy, postpartum hemorrhage, active smoke, passive smoke, alcohol use, primipara, baby gender, ways of delivery, mother's BMI, Gestational Weight Gain (GWG), and preeclampsia, First trimester(1st),Second trimester (2nd),Third trimester(3rd).

Table 5
The association between fruit consumption and LBW among underweight mothers in the 2010–2012 Lanzhou Birth Cohort Study (n = 1992).

Trimester	Amount of fruit intake(g/d)	NBW (n (%))	LBW + underweight BMI			
			n (%)	OR (95%CI)	aOR (95%CI)	$P^{\#}$
Before pregnancy	<200	1021 (57.5)	116 (65.3)	1.32 (0.93–1.86)	0.95 (0.57–1.59)	<0.0001
	200–350	567 (31.9)	49 (28.0)	reference	Reference	
	>350	188 (10.6)	10 (5.7)	0.62 (0.31–1.24)	0.50 (0.18–1.38)	
	P for trend	0.055				
1st	<200	466 (25.7)	67 (37.6)	1.34 (0.94–1.90)	1.34 (0.90–1.99)	<0.0001
	200–350	679 (37.4)	73 (41.0)	Reference	Reference	
	>350	672 (37.0)	38 (21.4)	0.53 (0.35–0.79)	0.64 (0.41–0.98)	
	P for trend	0.002				
2nd	<200	446 (24.5)	65 (36.3)	1.44 (1.01–2.05)	1.40 (0.95–2.07)	<0.0001
	200–400	741 (40.7)	75 (41.9)	Reference	Reference	
	>400	632 (34.7)	39 (21.8)	0.61 (0.41–0.91)	0.71 (0.46–1.09)	
	P for trend	0.025				
3rd	<200	437 (24.1)	64 (36.4)	1.45 (1.02–2.06)	1.49 (1.03–2.17)	<0.0001
	200–400	742 (40.9)	75 (42.6)	Reference	Reference	
	>400	634 (35.0)	37 (21.0)	0.58 (0.38–0.87)	0.67 (0.44–1.02)	
	P for trend	0.000				

Note: NBW: normal birth weight; LBW: low birth weight; BMI: body mass index; OR: odds ratio; aOR: adjusted odds ratio; CI: confidence interval. # adjusted P-values. The following confounders were controlled: whether attend pregnancy health care, first perinatal examination, age, education level, family's average monthly income, vaginal hemorrhage, natural pregnancy, postpartum hemorrhage, active smoke, passive smoke, alcohol use, primipara, baby gender, ways of delivery, mother's BMI, Gestational Weight Gain (GWG), and preeclampsia, First trimester(1st),Second trimester (2nd),Third trimester(3rd).

Table 6
The association between fruit intake and SGA among underweight mothers in the 2010–2012 Lanzhou Birth Cohort Study (n = 1992).

Trimester	Amount of fruit intake (g/d)	AGA (n (%))	SGA + underweight BMI			
			n (%)	OR (95%CI)	aOR (95%CI)	$P^{\#}$
Before pregnancy	<200	1024 (23.9)	118 (62.8)*	1.09 (0.78–1.52)	1.08 (0.76–1.55)	<0.0001
	200–350	559 (41.4)	59 (31.4) *	Reference	Reference	
	>350	187 (34.7)	11 (5.9) *	0.56 (0.29–1.08)	0.48 (0.22–1.04)	
	P for trend	0.005				
1st	<200	459 (25.4)	76 (39.4)	1.76 (1.24–2.50)	1.76 (1.19–2.61)	<0.0001
	200–350	690 (38.1)	65 (33.7)	Reference	Reference	
	>350	660 (36.5)	52 (26.9)	0.84 (0.57–1.22)	0.93 (0.61–1.42)	
	P for trend	0.000				
2nd	<200	441 (24.3)	72 (37.3)	1.62 (1.15–2.29)	1.66 (1.13–2.11)	<0.0001
	200–400	744 (41.1)	75 (38.9)	Reference	Reference	
	>400	627 (34.6)	46 (23.8)	0.73 (0.50–1.07)	0.80 (0.53–1.22)	
	P for trend	0.000				
3rd	<200	430 (23.9)	73 (37.8)	1.74 (1.23–2.45)	1.79 (1.21–2.64)	<0.0001
	200–400	747 (41.4)	73 (37.8)	Reference	Reference	
	>400	626 (34.7)	47 (24.4)	0.77 (0.53–1.13)	0.87 (0.57,1.34)	
	P for trend	0.000				

Note: AGA: appropriate for gestational age; SGA: small for gestational age; BMI: body mass index; OR: odds ratio; aOR: adjusted odds ratio; CI: confidence interval. # adjusted P-values. The following confounders were controlled: whether attend pregnancy health care, first perinatal examination, age, education level, family's average monthly income, vaginal hemorrhage, natural pregnancy, postpartum hemorrhage, active smoke, passive smoke, alcohol use, primipara, baby gender, ways of delivery, mother's BMI, Gestational Weight Gain (GWG), and preeclampsia, First trimester(1st),Second trimester(2nd),Third trimester(3rd).

infant LBW. For SGA, no significant association was found between excessive or inadequate fruit consumption and SGA births. However, after stratifying by the mother's pre-pregnancy BMI, the risk of infant LBW was only decreased with excessive fruit consumption in the 1st trimester of pregnancy. At the same time, it increased with inadequate fruit consumption in the 3rd trimester of pregnancy. On the other hand, the risk of SGA births increased with inadequate fruit consumption in the 1st, 2nd, and 3rd trimesters of pregnancy but showed no significant association with excessive fruit consumption.

The major finding of the present study is the protective role of fruit consumption on infant birth weight. Compared to adequate fruit consumption, excessive fruit consumption is associated with a decreased risk of infant LBW, while inadequate fruit consumption is associated with an increased risk of infant LBW. This finding is consistent with most previous studies showing a positive association between fruit consumption and infant birth weight. For instance, a Danish prospective cohort study [19] reported that the high levels of antioxidants and folic acid in fruits had beneficial effects on fetal growth. A case-control study in Spain also came to a similar conclusion and showed a positive correlation between dietary vitamin intake during pregnancy and newborn weight [40]. A prospective study in rural India also reported that the frequency of fruit consumption in the second trimester was related to neonatal weight, birth length, head circumference, and placental weight [24].

Several mechanisms can explain the link between increased fruit consumption and birth weight. First, prior research has demonstrated that the vitamin C contained in fruit may contribute to optimal placental functions and immune system functioning [10]. The risk of LBW can be significantly reduced by consuming fruits that are rich in nutrients such as antioxidant vitamins (C and E) and essential micronutrients (Cu and Zn) [41]. Second, oxidative stress is produced during placental development and peaks in the second trimester, which may lead to a series of adverse pregnancy outcomes, including LBW [41,42]. Consumption of fruits rich in antioxidant micronutrients greatly helps reduce oxidative stress and related adverse pregnancy outcomes such as LBW [43]. Third, a fruit-rich diet is known to lower blood pressure in pregnant women. Hypertension is the main risk factor for growth restriction, pregnancy complications, and adverse consequences (such as preeclampsia and SGA). Consumption of fruits may reduce the risk of LBW by reducing the risk of hypertension. Fourth, Saghafian et al.'s meta-analysis showed that fruit consumption was protective in preventing depression [44]. Since psychological distress such as depression and anxiety may also significantly restrict fetal development, fruit consumption may provide additional benefits to fetal growth and development by relieving psychological distress and improving the overall well-being of new mothers after delivery.

In our study, we failed to find any significant association between fruit consumption and SGA, which is consistent with the studies by Mitchell et al. [21], Ramon et al. [20], McCowan et al. [22], and Ricci et al. [23], but in contrast with the findings of Martínez-Galiano et al. [11,17], Rao et al. [24], and McCowan et al. [22]. However, stratified analysis by pre-pregnancy BMI showed that inadequate fruit consumption in the 1st, 2nd, and 3rd trimesters of pregnancy was associated with an increased risk of SGA births among pregnant women with underweight BMI. This finding indicates that the association between fruit consumption and SGA birth may be largely confounded by the pregnant women's pre-pregnancy BMI. Pre-pregnancy BMI has been well-established as an important predicting factor of SGA birth, as evidenced by Han et al.'s systematic review and meta-analyses on the effect of maternal underweight on baby birth weight [45]. The nutritional status before pregnancy is most evaluated by pre-pregnancy body mass index (BMI), with a low BMI indicating minimal maternal nutrient reserves [46]. However, being underweight is more preferred among women pre-pregnancy or during early pregnancy, and there is a decreasing trend of pre-pregnancy BMI among women of childbearing age in China [39]. Our study suggests that it is important to improve the BMI among underweight pregnant women while at the same time avoiding inadequate fruit consumption to reduce their risk of delivering SGA babies.

Furthermore, our study also showed that the beneficial effect of fruit consumption on newborn birth weight varied according to the different pregnancy trimesters of the intake, with a generally stronger effect observed in the later pregnancy. This finding added further support to previous research showing different nutritional requirements based on different pregnancy stages, with the highest nutritional demand occurring in the last stage with the fastest fetal growth [28,30,31]. Additionally, the more significant beneficial effect of fruit consumption in the later stages of pregnancy may reflect the cumulative effects of fruit consumption in the early stages of pregnancy, which warrants further research. Our findings suggest that fruit consumption should be initiated as soon as possible to achieve its maximum benefits, and appropriate fruit consumption recommendations should be developed based on different pregnancy trimesters.

Our study has several limitations. First, although this was a whole sample study, all participants were recruited from Gansu Province and may not represent pregnant women in other provinces, thus limiting the external validity of the current study findings. Second, our sample selection criteria were very general without excluding pregnant women with certain conditions that may affect LBW and SGA, such as placental disorders, fetal growth restriction, placental diseases, and planned premature births, though we did control some in our multivariate analysis. Future studies should use a more selective sample, excluding pregnant women with the abovementioned conditions, to reach a more robust conclusion. Third, although the FFQ was scientifically developed, it has not been formally validated and may need further validation against other standard dietary scales in future studies. Fourth, there is no detailed information about fruit categories in the FFQ and thus; thus, the role of each specific type of fruit cannot be determined. Fifth, fruit consumption for pregnant women on the FFQ was based on a single 24-h recall, which may not be sufficient to determine typical daily intake. However, a well-trained dietitian used a standard protocol to help subjects recall their daily diet, thereby minimizing any potential deviations [10]. Sixth, we could not measure or control the organophosphorus insecticides that may exist in the fruits, which are associated with shortened gestation and reduced birth weight [47,48]. Seventh, we did not include other potential confounders, such as physical activity and dietary supplements. Future studies may also consider adding these factors for adjustment.

The strengths of our study include the sample representativeness and quality of data. First, Gansu province is located in the northwest of China, with the lowest economic development, and thus can represent the less developed areas in China, which were often under-researched. Second, we collected maternal anthropometry and accurate gestational age from one year before and throughout the pregnancy. Our study observation period is much longer than most previous studies that have focused on only one small pregnancy period, such as 1st or 3rd trimester of pregnancy. As a result, our study provides a more comprehensive and reliable evaluation of the association between maternal fruit consumption and fetal growth. Third, our assessment of fruit consumption was based on FFQ, which asks participants' food consumption by various food groups as well as nutrient intakes. As a result, the FFQ provides an objective and reliable assessment of fruit consumption, unlike most previous studies, which are based on one simple self-reported question on whether they have consumed any fruit during pregnancy [14,49].

5. Conclusions

In conclusion, our study showed that fruit consumption during pregnancy was associated with a reduced risk of LBW. For SGA, inadequate fruit consumption was associated with an increased risk of SGA only among pregnant women with underweight BMI. Our findings provide helpful guidance for future antenatal dietary interventions to focus on improving fruit consumption during pregnancy to improve fetal growth and development and reduce the risk of LBW and SGA. Future studies should also consider validating our findings in a more selective sample using more reliable assessment tools and controlling more confounders.

Ethics declarations

This study was reviewed and approved by [the Institutional Review Board of Gansu Provincial Maternity and Child Care Hospital] with the approval number: [5], dated [December 19, 2012].

Data availability statement

Data will be made available on request.

Funding

This work was supported by National Natural Science Foundation of Gansu Province (grant number: 23JRRA1392) and National Natural Science Foundation of Gansu Province (grant number: 22JR5RA725).

CRediT authorship contribution statement

Rongrong Xu: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Yali Liu:** Supervision. **Hongmei Cui:** Data curation. **Xinin Xu:** Software. **Fang Wang:** Resources. **Zhaoyan Meng:** Supervision. **Qing Liu:** Writing – review & editing, Visualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Rongrong Xu reports financial support was provided by National Natural Science Foundation of Gansu Province. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e35628.
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