Maternal vitamin D deficiency during pregnancy elevates the risks of small for gestational age and low birth weight infants in Chinese population

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***Key terms*:** Maternal vitamin D deficiency, a population-based birth cohort study, small for gestational age, low birth weight

CONTEXT: Vitamin D deficiency is common in the pregnant women. Nevertheless, the association between maternal vitamin D status during pregnancy and the risks of small for gestational age (SGA) and low birth weight (LBW) infants is uncertain.

OBJECTIVE: The objective of this study was to investigate whether maternal vitamin D deficiency during pregnancy and the risks of SGA and LBW infants in Chinese population.

DESIGN AND PARTICIPANTS: This study was a population-based birth cohort study that recruited total 3658 eligible mother-and-singleton-offspring pairs.

MAIN OUTCOME MEASURES: Serum 25(OH)D was measured by radioimmunoassay. The rate and relative risk (RR) for SGA and LBW infants were calculated among subjects with vitamin D deficiency and insufficiency during pregnancy.

Results: There was a positive correlation between maternal serum 25(OH)D level and offspring birth weight ($r=0.477$, $P<0.001$). Further analysis showed that 4.98% neonates were LBW infants among subjects with vitamin D deficiency (RR: 12.00; 95%CI: 4.37, 33.00) and 1.32% among subjects with vitamin D insufficiency (RR: 3.18; 95%CI: 1.07, 9.48). After adjustment for confounders, RR for LBW infants was 12.31 (95%CI: 4.47, 33.89) among subjects with vitamin D deficiency and 3.15 (95%CI: 1.06, 9.39) among subjects with vitamin D insufficiency. Moreover, 16.01% neonates were SGA infants among subjects with vitamin D deficiency (RR: 5.72; 95%CI: 3.80, 8.59) and 5.59% among subjects with vitamin D insufficiency (RR: 1.99; 95%CI: 1.27, 3.13). After adjustment for confounders, RR for SGA infants was 6.47 (95%CI: 4.30, 9.75) among subjects with vitamin D deficiency and 2.01 (95%CI: 1.28, 3.16) among subjects with vitamin D insufficiency.

CONCLUSION: Maternal vitamin D deficiency during pregnancy elevates the risks of SGA and LBW infants in Chinese population.

Vitamin D, a secosteroid hormone known for its classical functions in calcium uptake and bone metabolism (1), is now well recognized for its nonclassical actions including modulation of innate immune response and regulation of cell proliferation (2–5). Vitamin D deficiency, defined as lower than 50 nmol/L of 25(OH)D, is common in the pregnant women and is increasingly recognized as a global public health problem (6, 7). Increasing evidence demonstrates that vitamin D deficiency during pregnancy is linked with gestational diabetes mellitus, preeclampsia and bacterial vaginosis (8–10). Moreover, maternal vitamin D deficiency during pregnancy is asso-

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ciated with the reduced bone-mineral content, the impaired muscle development, the increased asthma and schizophrenia in adult offspring (11–15).

Intrauterine growth restriction (IUGR), which manifests as small for gestational age (SGA) and low birth weight (LBW), increases the risk of infant morbidity and metabolic diseases in adulthood (16, 17). Recently, several small epidemiological studies explored the association between vitamin D status during pregnancy and SGA and LBW infants with contradictory results (18–21). Until now, no report analyzed the association between vitamin D status at different gestational stages and the risk of SGA and LBW infants. Therefore, the association between maternal vitamin D status at different gestational stages and the risks of LBW and SGA infants needs to be further determined in a large longitudinal investigation.

The objective of the present study was to analyze whether maternal vitamin D deficiency at different gestational stages elevates the risks of LBW and SGA infants in a Chinese population-based birth cohort study. Our results demonstrate that maternal vitamin D deficiency not only at the first trimester but also at middle and late gestational stages elevates the risks of LBW and SGA infants in Chinese population.

Subjects and Methods

Cohort study

The China-Anhui Birth Cohort Study (C-ABCS) is a prospective population-based cohort study that recruited 16 766 pregnant women from six major cities of Anhui province in China between November 2008 and October 2010. Total 13 454 singleton live births were followed up from this cohort (22). The present study analyzed a subsample of the C-ABCS cohort that recruited 4358 pregnant women from Hefei city of Anhui province between January 2009 and December 2009. For this study, eligible participants were mother-and-singleton-offspring pairs in which serum samples from mothers were available for analysis of 25(OH)D and offspring had a detailed birth records. Thirty-six pregnant women giving birth to twins, 15 fetal deaths, 2 stillbirths, 58 abortions and 589 withdrew were excluded from this study. Total 3658 mother-and-singleton-offspring pairs were eligible for this study. The demographic characteristics of pregnant women from mother-offspring pairs are presented in Table 1. No subject was drinking alcohol or smoking cigarette throughout pregnancy. The present study obtained ethics approval from the ethics committee of Anhui Medical University. Oral and written consents were obtained from all pregnant women.

Definition of SGA and LBW

In this study, SGA births were live-born infants that were < 10th percentile of birth weight according to nomograms based

Table 1. Maternal demographic characteristics

Characteristics	Variables
Pregnant women (n)	3658
Maternal age [years, means ± SD]	27.5 ± 3.2
<25 [n (%)]	579 (15.83)
25− [n (%)]	1137 (81.08)
35− [n (%)]	113 (3.09)
Maternal BMI [kg/m^2, n (%)]	
<18.5	788 (21.54)
18.5−	2754 (75.29)
25.0−	116 (3.17)
Season of blood sample [n (%)]	
Spring (March--May)	1341 (36.66)
Summer (June--August)	822 (22.47)
Fall (September--November)	755 (20.64)
Winter (December--February)	740 (20.23)
Periconceptional multivitamin use [n (%)]	
No	3053 (83.46)
Less than one month	291 (7.96)
More than one month	314 (8.58)
Family monthly income (RMB/yuan) [n (%)]	
Low (<2000)	1655 (45.24)
Middle (2000−)	1483 (40.54)
High (4000−)	520 (14.22)
Parity [n(%)]	
1	3510 (95.95)
>1	148 (4.05)
Gestational week of blood sample [wk, n (%)]	
First-trimester (<13)	1284 (35.10)
Second-trimester (13−)	2268 (62.00)
Third-trimester (28−)	106 (2.90)

on gender and gestational age from a reference population of 13 454 infants delivered at C-ABCS (23). LBW births were live-born infants that were < 2500 g in birth weight.

Measurement of 25(OH)D

Maternal nonfasting blood samples taken as part of routine antenatal care were collected and stored initially at –20°C, and then at −80°C, with no further freeze-thaw cycles, until 25(OH)D measurement. Serum samples could be from any stage of pregnancy. Serum 25(OH)D was measured by Radioimmunoassay (RIA) using a kit from Diasorin (DiaSorin Inc, Stillwater, MN, USA) following manufacturer's instructions (24). Serum 25(OH)D level is expressed as ng/ml. The quality and reproducibility was determined using the quality controls provided with the kits. Two controls (low control: 14.1 ng/ml; high control: 54.1 ng/ml) were provided and the coefficient of variation for all kits used was 16.07% for the low control and 13.48% for the high control. The controls fell within the acceptable range given by the manufacturer.

Statistical analysis

We used means (SD or 95%CI) and proportions to describe all variables for included mothers and offspring. The differences between included mother-and-offspring pairs and those excluded because of missing data were investigated with *t* tests for continuously measured variables (with those variables that were right-skewed being logged) and χ^2 tests for categorical variables. Pearson's correlation coefficients were used to assess whether maternal serum 25(OH)D levels were correlated with offspring birth weight. Linear regression was used to explore the association between birth weight (dependent variables) and maternal serum 25(OH)D level during pregnancy (independent variables): model A was minimally adjusted (included BMI before pregnancy, maternal age and season of blood sample); model B was the main confounder-adjusted model, and was model A plus adjustment for maternal socio-economic status, maternal periconceptional multivitamin use and parity (25). Maternal serum 25(OH)D level was divided into three groups according to following criteria: 25(OH)D < 20 ng/ml (50 nmol/l) for vitamin D deficiency, 25(OH)D 20–29.9 ng/ml (50–75 nmol/l) for vitamin D insufficiency, and 25(OH)D ≥ 30 ng/ml (75 nmol/l) for vitamin D sufficiency (6). The rate and relative risk (RR) of LBW and SGA infants were calculated among different groups. For adjustment of maternal BMI before pregnancy, maternal age, season and gestational week of blood sample, multiple logistic regression model was used to calculate adjusted RR with 95% confidence intervals (95% CI) with respect to LBW and SGA ininfants. A *p*-value of < 0.05 (two-tailed) or a 95% CI not including the null point (for linear regression) or 1 (for logistic regression and RR) was considered statistically significant.

Results

Correlation between maternal serum vitamin D level during pregnancy and birth weight

The correlation between maternal serum 25(OH)D level during pregnancy and birth weight were analyzed. As shown in Figure 1, there was a positive correlation between maternal serum 25(OH)D level and birth weight (r = 0.477, $P < .001$). Further analysis showed that there was a threshold (about 40 ng/ml) below which maternal serum 25(OH)D level is an important predictor for offspring birth weight. Linear regression was used to further explore the correlation between maternal serum 25(OH)D level during pregnancy and birth weight. After minimal adjustment for BMI before pregnancy, maternal age, and season of blood sample (Model A), maternal serum 25(OH)D level, as a continuous variable, was a significant predictor of birth weight with each additional 1 ng/ml 25(OH)D associated with an additional 23.87 g of birth weight (Figure 2). After further adjustment for main confounders including model A plus adjustment for maternal socio-economic status and parity (Model B), mean difference was 23.66 g in birth weight per 1 ng/ml 25(OH)D (Figure 2).

Association between vitamin D status during pregnancy and the risks of LBW and SGA infants

The rate and RR of SGA was analyzed. As shown in Table 3

Association between vitamin D status at early gestational stage and the risks of LBW and SGA infants

The association between vitamin D status at the first trimester and the risk of SGA infants was analyzed. As

Table 2. The distribution of maternal 25(OH)D levels during pregnancy and its correlation with birth weight

Serum 25(OH)D3 (ng/ml)	n	Cumulative Percentage (%)	Birth Weight (g, 95%CI)
<10	46	1.26	2430.1 (2249.9, 2610.3)
10−	303	9.54	3095.8 (3049.6, 3142.1)
15−	1056	38.41	3244.1 (3218.8, 3269.4)
20−	545	53.31	3292.5 (3261.6, 3323.5)
25−	744	73.65	3499.9 (3472.0, 3527.7)
30−	488	86.99	3614.2 (3577.6, 3650.7)
35−	273	94.45	3789.5 (3743.8, 3835.2)
40−	99	97.16	3804.2 (3729.3, 3879.1)
45−	49	98.50	3779.0 (3659.0, 3899.0)
50−	55	100.00	3793.5 (3685.4, 3901.6)

shown in Table 4, 15.94% neonates were SGA infants among subjects with vitamin D deficiency and 6.11% among subjects with vitamin D insufficiency, significantly higher than 2.10% among subjects with vitamin D sufficiency. RR for SGA infants was 7.61 (95%CI: 3.47, 16.67) among subjects with vitamin D deficiency and 2.92 (95%CI: 1.25, 6.77) among subjects with vitamin D insufficiency. Adjusted RR for SGA infants was 8.75 (95%CI: 3.98, 19.22) among subjects with vitamin D deficiency and 2.99 (95%CI: 1.29, 6.96) among subjects with vitamin D insufficiency using multiple logistic regression model. The association between vitamin D status at the first trimester and the risk of LBW infants was then analyzed. As shown in Table 4, 4.53% neonates were LBW infants among subjects with vitamin D deficiency and 0.90% among subjects with vitamin D insufficiency, significantly higher than 0.30% among subjects with vitamin D sufficiency. RR for LBW infants was 15.12 (95%CI: 2.03, 112.51) among subjects with vitamin D deficiency and 3.02 (95%CI: 0.34, 27.17) among subjects with vitamin D insufficiency. Adjusted RR for LBW infants was 15.03 (95%CI: 2.01, 112.15) among subjects with vitamin D deficiency and 2.95 (95%CI: 0.33, 26.54) among subjects with vitamin D insufficiency using multiple logistic regression model.

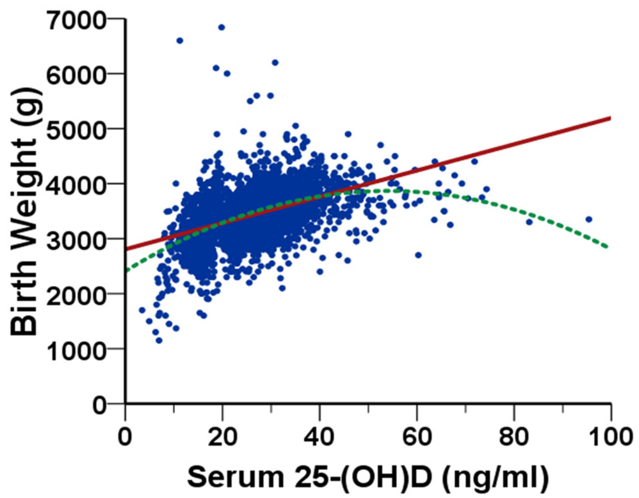

Figure 1. Correlation between maternal 25(OH)D level during pregnancy and birth weight. Serum 25(OH)D level during pregnancy was assessed among 3658 pregnant women. Correlation between maternal serum 25(OH)D level and birth weight was analyzed. Correlation coefficient r = 0.477, *P* < .001.

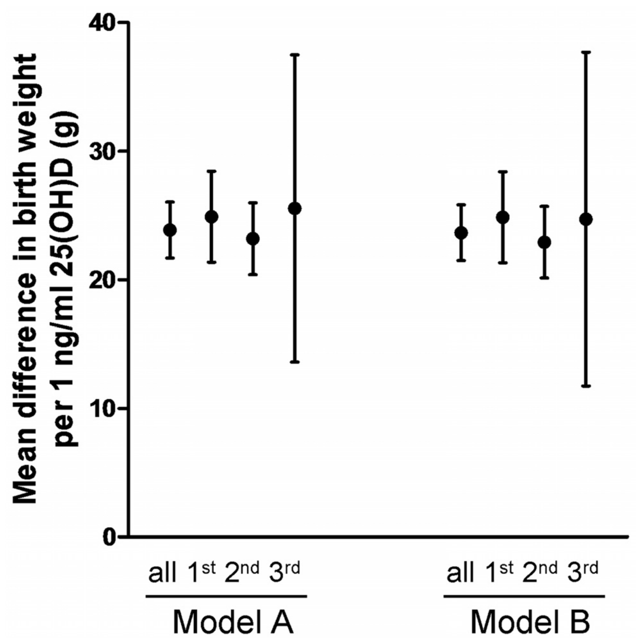

Figure 2. Mean difference in birth weight in relation to maternal serum 25(OH)D level during pregnancy. Linear regression was used to explore the association between birth weight (dependent variables) and maternal serum 25(OH)D level during pregnancy (independent variables): Model A was minimally adjusted (included BMI before pregnancy, maternal age and season of blood sample); Model B was further adjustment for main confounders, and was model A plus adjustment for maternal socio-economic status and parity. First, First-trimester (n = 1284); second, Second-trimester (n = 2268); third, Third-trimester (n = 106); all, first + second + third (n = 3658). Data are mean difference (mean, 95% CI) in birth weight.

Association between vitamin D status at middle and late gestational stages and the risks of LBW and SGA infants

The association between vitamin D status on the second and third trimesters and the risk of SGA infants was analyzed. As shown in Table 4, 16.05% neonates were SGA infants among subjects with vitamin D deficiency and 5.31% among subjects with vitamin D insufficiency, significantly higher than 3.17% among subjects with vitamin D sufficiency. RR for SGA infants was 5.06 (95%CI: 3.13, 8.16) among subjects with vitamin D deficiency and 1.67 (95%CI: 0.98, 2.86) among subjects with vitamin D insufficiency. Adjusted RR for SGA infants was 5.58 (95%CI: 3.45, 9.04) among subjects with vitamin D deficiency and 1.65 (95%CI: 0.97, 2.83) among subjects with vitamin D insufficiency using multiple logistic regression model. The association between vitamin D status on the second and third trimesters and the risk of LBW infants was then analyzed. As shown in Table 4, 5.24% neonates were LBW infants among subjects with vitamin D deficiency and 1.53% among subjects with vitamin D insufficiency, significantly higher than 0.48% among subjects with vitamin D sufficiency. RR for LBW infants was 11.00 (95%CI: 3.41, 35.51) among subjects with vitamin D deficiency and 3.22 (95%CI: 0.92, 11.36) among subjects with vitamin D insufficiency. Adjusted RR for LBW infants was 11.03 (95%CI: 3.41, 35.68) among subjects with vitamin D deficiency and 3.18 (95%CI: 0.90, 11.23) among subjects with vitamin D insufficiency using multiple logistic regression model.

Table 3. Association between Maternal vitamin D status and its association with LBW and SGA

	Maternal vitamin D status during pregnancy [1]			
	Deficiency	**Insufficiency**	**Sufficiency**	P_{trend}
Mother-offspring pairs eligible [n (%)]	**1405 (38.41)**	**1289 (35.24)**	**964 (26.35)**	
Rate and relative risk for low birth weight (LBW)				
Infants with LBW (n)	70	17	4	
Rate for LBW (%)	4.98	1.32	0.41	<0.001
Unadjusted RR for LBW (95% CI)	12.00 (4.37, 33.00)	3.18 (1.07, 9.48)	1.00	<0.001
Adjusted RR for LBW (95% CI) [2,3]	12.31 (4.47, 33.89)	3.15 (1.06, 9.39)	1.00	<0.001
Rate and relative risk for small for gestational age (SGA)				
Infants with SGA (n)	225	72	27	
Rate for SGA (%)	16.01	5.59	2.80	<0.001
Unadjusted RR for SGA (95% CI)	5.72 (3.80, 8.59)	1.99 (1.27, 3.13)	1.00	<0.001
Adjusted RR for SGA (95% CI) [2,4]	6.47 (4.30, 9.75)	2.01 (1.28, 3.16)	1.00	<0.001

[1] 25(OH)D <20 ng/ml for deficiency; 20 ≤ 25(OH)D<30 ng/ml for insufficiency; 25(OH)D≥30 ng/ml for sufficiency.

[2] Adjusted for BMI before pregnancy, maternal age, season and gestational week of blood sample.

[3] Dependent variables: LBW (yes or no); Independent variables: Maternal vitamin D status (sufficiency, insufficiency and deficiency)

[4] Dependent variables: SGA (yes or no); Independent variables: Maternal vitamin D status (sufficiency, insufficiency and deficiency)

Discussion

In the cohort study, no subject was smoking cigarette, pre-eclampsia or drinking alcohol throughout pregnancy (data not shown). Several reports show that maternal age, season of sampling influences maternal vitamin D status during pregnancy (26, 27). In the present study, maternal age, family monthly income, parity and gestational week of blood sample, did not influence serum 25(OH)D level during pregnancy. By contrast, serum 25(OH)D level was slightly higher among subjects with BMI18.5–24.9 than those of subjects with either BMI < 18.5 or BMI ≥ 25.0. Moreover, serum 25(OH)D level was increased among multivitamin users. As expected, serum 25(OH)D level during pregnancy was slightly higher in the spring and summer than in the fall and winter.

The present study analyzed the association between maternal vitamin D status during pregnancy and birth weight in a Chinese population-based birth cohort study that recruited total 3658 eligible mother-and-singleton-offspring pairs. We demonstrated that there was a positive correlation between maternal serum 25(OH)D level and birth weight in Chinese population ($r = 0.477$, $P < .001$). Further analysis showed that there was a threshold of about 40 ng/ml below which maternal serum 25(OH)D level is an important predictor for birth weight in offspring. After adjustment for main confounders, such as BMI before pregnancy, maternal age, maternal socio-economic status, parity, and season of blood sample, maternal serum 25(OH)D level, as a predictor of birth weight, was with each additional 1 ng/ml 25(OH)D in maternal serum associated with an additional 23.66 g birth weight in offspring. These results provide a strong evidence that maternal vitamin D status during pregnancy is associated with intrauterine fetal growth in offspring.

It remains uncertain whether maternal vitamin D deficiency during pregnancy elevates the risks of SGA and LBW infants. Several studies explored the association between maternal vitamin D status during pregnancy and the risks of SGA and LBW infants with contradictory results. Some reports showed that there was no association between maternal serum 25(OH)D level and child's body size and birth weight (18, 19). Other studies found that maternal vitamin D status during pregnancy was associated with the risk of SGA infants (20, 21). The inconsistency of past findings may be related to following reasons: first, negative results came most frequently from small samples (18, 19); second, maternal vitamin D status during pregnancy is a link to ethnic disparities in adverse birth outcomes (20, 21). The present study analyzed the association between maternal vitamin D status during pregnancy and the risks of SGA and LBW infants in Chinese population. Our results showed that 4.98% neonates were LBW infants among subjects with vitamin D deficiency (RR: 12.00; 95%CI: 4.37, 33.00) and 1.32% among subjects with vitamin D insufficiency (RR: 3.18; 95%CI: 1.07, 9.48). Moreover, 16.01% neonates were SGA infants among subjects with vitamin D deficiency (RR: 5.72; 95%CI: 3.80, 8.59) and 5.59% among subjects with vitamin D insufficiency (RR: 1.99; 95%CI: 1.27, 3.13). To our knowledge, the present study is the first to demonstrate that maternal vitamin D deficiency during pregnancy elevates the risks of LBW and SGA infants in a Chinese population-based birth cohort study.

Most past studies analyzed the association between maternal vitamin D status at the first trimester and the risks of SGA and LBW infants (28, 29). The present study analyzed the association between maternal vitamin D status at different gestational stages and the risks of SGA and LBW infants. On the first trimester, 4.53% neonates were LBW infants among subjects with vitamin D deficiency (RR: 15.12; 95%CI: 2.03, 112.51) and 0.90% among subjects with vitamin D insufficiency (RR: 3.02; 95%CI: 0.34, 27.17). Moreover, 15.94% neonates were SGA infants among subjects with vitamin D deficiency (RR: 7.61; 95%CI: 3.47, 16.67) and 6.11% among subjects with vitamin D insufficiency (RR: 2.92; 95%CI: 1.25, 6.77). On the second and third trimesters, 5.24% neonates were LBW infants among subjects with vitamin D deficiency (RR: 11.00; 95%CI: 3.41, 35.51) and 1.53% among subjects with vitamin D insufficiency (RR: 3.22; 95%CI: 0.92, 11.36). In addition, 16.05% neonates were SGA infants among subjects with vitamin D deficiency (RR: 5.06; 95%CI: 3.13, 8.16) and 5.31% among subjects with vitamin D insufficiency (RR: 1.67; 95%CI: 0.98, 2.86). These results suggest that maternal vitamin D deficiency not only at early but also a middle and late gestational stages elevates the risks of SGA and LBW infants.

The mechanism through which vitamin D deficiency during pregnancy elevates the risks of SGA and LBW infants remains obscure. Increasing evidence demonstrates that vitamin D has an anti-inflammatory activity (30, 31). A recent study showed that vitamin D receptor plays a pivotal role in regulating placental inflammation (2). Indeed, numerous reports found that maternal and placental inflammation was associated with fetal IUGR in rodent animals (31, 32). An earlier investigation showed that serum IL-8 and TNF-α levels were significantly increased in preeclamptic patients with IUGR infants but not in preeclamptic patients with normal infants (33). Another study found that there was a strong association between placental inflammation and the incidence of LBW infants in preterm newborns (34). According to a recent report, chronic inflammations including chronic villitis and chronic chorioamnionitis could be detected in placentas from pregnant women with IUGR infants (35). These results suggest that placental inflammation was also linked with fetal IUGR in human beings. Further research is necessary to investigate the association among vitamin D status during pregnancy, placental inflammation and the risks of SGA and LBW infants.

An earlier human study found that a correlation between serum vitamin D and IGF-1 concentration (36). A recent study showed that vitamin D supplementation increases the production of IGF-1 in adults (37). Indeed, numerous reports demonstrated that mutations or targeted deletions of the IGF ligands IGF1 and IGF2, as well as the down-regulation of IGF-1 signaling pathway lead to fetal IUGR in humans and rats (38, 39). Further research is necessary to investigate whether maternal vitamin D deficiency cause fetal IUGR through decreasing production of IGF-1 and IGF-2 in animal experiments.

The present study laid emphasis on whether maternal vitamin D deficiency elevated the risk of SGA and LBW in Chinese population. However, the present study has several limitations. First, only a single sample at different seasons and gestational ages was analyzed in the present study. Second, the present study did not clarify the mechanism why maternal vitamin D deficiency during pregnancy elevated the risks of LBW and SGA infants. The mechanism by which maternal vitamin D deficiency during pregnancy induces LBW and SGA needs to be explored in animal experiments.

In summary, the present study analyzed the association between maternal serum 25(OH)D level at different gestational stages and the risks of SGA and LBW infants in a Chinese population-based birth cohort study. We observed a positive correlation between maternal serum 25(OH)D level during pregnancy and birth weight in offspring. Our results demonstrate that maternal vitamin D deficiency, not only at early but also middle and late gestational stages, elevates the risks of SGA and LBW infants in Chinese population. The present study provide an important evidence that maternal vitamin D supplementation during pregnancy should be recommended in Chinese population.

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Competing Interests: The authors have declared that no competing interests exist.

Table 4. The incidence and relative risk (*RR*) for LBW and SGA infants based on maternal vitamin D status in different trimesters

	Maternal vitamin D status during pregnancy [1]			
	Deficiency	Insufficiency	Sufficiency	P_{trend}
		First trimester [2]		
LBW				
Infants (n)	508	442	334	
Infants with LBW (n)	23	4	1	
Rate for LBW (%)	4.53	0.90	0.30	<0.001
Unadjusted RR for LBW (95% CI)	15.12 (2.03, 112.51)	3.02 (0.34, 27.17)	1.00	<0.001
Adjusted RR for LBW (95% CI) [3,4]	15.03 (2.01, 112.15)	2.95 (0.33, 26.54)	1.00	<0.001
SGA				
Infants (n)	508	442	334	
Infants with SGA (n)	81	27	7	
Rate for SGA (%)	15.94	6.11	2.10	<0.001
Unadjusted RR for SGA (95% CI)	7.61 (3.47, 16.67)	2.92 (1.25, 6.77)	1.00	<0.001
Adjusted RR for SGA (95% CI) [3,5]	8.75 (3.98, 19.22)	2.99 (1.29, 6.96)	1.00	<0.001
Second and third trimester [2]				
LBW				
Infants (n)	897	847	630	
Infants with LBW (n)	47	13	3	
Rate for LBW (%)	5.24	1.53	0.48	<0.001
Unadjusted RR for LBW (95% CI)	11.00 (3.41, 35.51)	3.22 (0.92, 11.36)	1.00	<0.001
Adjusted RR for LBW (95% CI) [3,4]	11.03 (3.41, 35.68)	3.18 (0.90, 11.23)	1.00	<0.001
SGA				
Infants (n)	897	847	630	
Infants with SGA (n)	144	45	20	
Rate for SGA (%)	16.05	5.31	3.17	<0.001
Unadjusted RR for SGA (95% CI)	5.06 (3.13, 8.16)	1.67 (0.98, 2.86)	1.00	<0.001
Adjusted RR for SGA (95% CI) [3,5]	5.58 (3.45, 9.04)	1.65 (0.97, 2.83)	1.00	<0.001

[1] 25(OH)D<20 ng/ml for deficiency; 20 ≤ 25(OH)D<30 ng/ml for insufficiency; 25(OH)D≥30 ng/ml for sufficiency.

[2] First trimester: gestational week <13 week; Second and third trimester: gestational week ≥13 week.

[3] Adjusted for BMI before pregnancy, season of blood sample and maternal age.

[4] Dependent variables: LBW (yes or no); Independent variables: Maternal vitamin D status during pregnancy (sufficiency, insufficiency and deficiency)

[5] Dependent variables: SGA (yes or no); Independent variables: Maternal vitamin D status during pregnancy (sufficiency, insufficiency and deficiency)

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