Prevalence of Vitamin D Deficiency during Second Trimester of Pregnancy in Shanghai China, Risk Factors and Effects on Pregnancy Outcomes

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Abstract
Background: Vitamin D plays important roles in various physiological processes. Vitamin D deficiency is common among pregnant women in some regions, such as China. Our study aimed to determine the prevalence of Vitamin D deficiency during second trimester of pregnancy in Shanghai China, and explore its risk factors and effects on pregnant outcomes.

Methods: Overall, 23100 pregnant women (2013 to 2017, Shanghai, China) were included and vitamin D concentrations were measured at 16 weeks of gestation. Correlations between vitamin D concentrations and participants’ general data and maternal and infant outcomes were analyzed by chi square test. Non-conditional multivariate logistic regression analysis was used to screen the independent risk factors for vitamin D deficiency.

Results: Vitamin D deficiency was significantly correlated with aging, education level, smoking, dirking, BMI before pregnancy, body weight gain during pregnancy \((P<0.01)\), the use of vitamin D supplement and milk consumption, and older than 30 years, drinking, smoking, BMI before pregnancy \(> 36\), body weight gain during pregnancy \(< 40\)g per day, no daily milk consumption, no vitamin D supplement, and education lever below college were independent risk factors for vitamin D deficiency in second trimester of pregnancy. In addition, vitamin D deficiency in second trimester of pregnancy was closely correlated with the occurrence of a serious of adverse maternal and infant outcomes.

Conclusion: Vitamin D deficiency was still common among women in second trimester of pregnancy in Shanghai China. Vitamin D deficiency was closely correlated with the occurrence of a serious of adverse maternal and infant outcomes.

Keywords: Vitamin D deficiency; Second trimester of pregnancy; Prevalence; Risk factor; Pregnant outcome

Introduction

Vitamin D deficiency is a widespread public health problem worldwide. In China, the rapid economic development and the shift of diet behaviors to Western style in past several decades significantly increased the prevalence of many types of chronic diseases, including vitamin D deficiency \((1, 2)\). Vitamin D deficiency is considered to be common in pregnant women \((3, 4)\), and is closely correlated with the a serious of serious short- and long-term health problems in offspring, including skeletal problems, impaired growth, asthma type 1 diabetes, schizophrenia and so on \((5)\). Therefore, prevention of vitamin D deficiency is a key in improving maternal and infant outcomes.

Problems with urbanization, such as air pollution, less physical activity and increased sedentary occupations have been proved to be at least partial-
ly responsible for the increased prevalence of vitamin D deficiency in developed countries and areas (6). Besides that, increased incidence of obesity in recently years may also a major cause of high increased prevalence of vitamin D due to the dependency of vitamin D status on body mass index (BMI) (7). Shanghai is one of the most developed areas in China, and a considerable proportion of females in this area were occupied by sedentary jobs, which inevitably increases the incidence of vitamin D deficiency and adverse pregnancy events such as miscarriage (8). Vitamin D status of residents in Shanghai has been reported by a previous study (9). However, it has been 5 years since this report, and the effects of vitamin D deficiency on maternal and infant outcomes, especially in the second trimester of gestation were not reported.

We aimed to update the information of the prevalence of vitamin D deficiency during second trimester of pregnancy in Shanghai, China, and to explore its risk factors of vitamin D deficiency during second trimester and its effects on pregnant outcomes.

Materials and Methods

Subjects
A total of 23100 pregnant women were recruited from January 2013 to October 2017 (in winter timer) in Shanghai Changning District Maternal and Child Health Hospital, Shanghai, China. The age of those patients ranged from 22 to 44 yr, with an average age of 32±4.2 years. Manual workers and the ones with kidney disease, chronic liver disease, severe cardiocerebral vascular disease, or cancer were excluded. Patients with a history of diabetes mellitus were also not included.

This study was approved by the Ethics Committee of Shanghai Changning District Maternal and Child Health Hospital. All participants signed informed consent.

Measurement of blood 25OHD and grouping
Blood was extracted from each participant by venipuncture at 16 weeks of gestation. OCTEIA 25-Hydroxy vitamin D kit (Immunodiagnostic Systems Limited, UK) was used to determine serum 25OHD concentration. Patients were divided into different groups according to Institute of Medicine (IOM) cut-offs: serum 25(OH)D <30 nmol/L, deficiency; between 30–50 nmol/L, inadequacy; and >50 nmol/L, sufficiency (9).

Data collection
Participants were interviewed face to face to obtain their basic formations. Smoking habits were grouped into “none” (never smoking), “light” (nor more 70 cigarettes/week), and “heavy” (70 cigarettes or more per week). Alcohol intake were classified into “none” (never drinking during past 1 year), “light” (drinking sporadically), and “heavy” (drinking every more than 3 days a well). Other information, such as age, education level, the use of vitamin D supplement and consumption of milk products were also collected. BMI was calculated and body weight gain during pregnancy was recorded.

Determination of maternal and infant outcomes
Gestational hypertension was defined as new onset hypertension (ystolic blood pressure (BP) ≥ 140 mmHg and/or diastolic BP >=90 mmHg measured twice 4 hours apart) at more than 20 weeks of gestation. Diagnostic criteria for gestational diabetes mellitus: normal 75gOGTT; fasting blood glucose <5.1mmol/L; blood glucose at 1h after glucose uptake (75g) <10.0 mmol/L; blood glucose at 2 h after glucose uptake (75g) <8.5 mmol/L, patients with any abnormal index were diagnosed as gestational diabetes mellitus. Pre-eclampsia was defined as new onset hypertension after 20 weeks of gestation combined with proteinuria (>0.3 g/day or >=2+ dipstick), or haemolysis, or eclampsia, low platelets, and elevated liver enzymes (HELLP syndrome), or new onset of proteinuria, on the background of essential hypertension. Adverse placental outcomes were determined and included pre-eclampsia, gestational hypertension, intrauterine fetal death, placental abortion and so on.

Statistical analysis
SPSS 17.0 statistical software (Chicago, IL, USA) was used for all statistical analysis. Measurement

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data were expressed by $\bar{x} \pm s$ and compared by $t$ test. Count data were by $\chi^2$ test. Indicators with statistical significance among vitamin D deficiency group, inadequacy group and sufficiency group were assigned values and set as independent variables. Age<=$30$ yr, 0; Age>$30$, 1; education level $>$college, 0; education level $<=$college, 1; consume milk products daily, 0; not consume milk products daily, 1; for smoking and drinking habit, none, 0; light, 1; heavy 2; BMI $<=$26, 0; BMI $>$26, 1; body weight gain $>$40g/day, 0; body weight gain $<$40 g/day, 1. Non-conditional multivariate logistic regression analysis was used to screen the independent risk factors for vitamin D deficiency.

## Results

### Correlations between vitamin D status and general data of pregnant women

Overall, 23100 pregnant women were included. Among them, 7526 females showed vitamin D deficiency, accounting for 32.58%, and 7649 females showed vitamin D inadequacy, accounting for 33.11%. As shown in Table 1, vitamin D status was significantly correlated with age, education level, smoking habit, drinking habit, BMI, body weight gain, the use of vitamin D supplement and consumption of milk ($P<0.01$). However, vitamin D status was not closely correlated with race.

![Table 1: Correlations between vitamin D status and general data of pregnant women](image)

**Analysis of risk factors for vitamin D deficiency**

Non-conditional multivariate logistic regression analysis was used to identify independent risk factors for vitamin D deficiency. Older than 30 years, drinking, BMI before pregnancy $>$26, body weight gain during pregnancy $<$40g/day, smoking, none-daily milk consumption, none-vitamin D supplement, and education level below college were independent risk factors for vitamin D deficiency ($P<0.05$).
Table 2: Analysis of risk factors for vitamin D deficiency

| Factors                                      | Regression coefficient | Standard error | Wald value | Odd ratio | 95% confidence interval | P value |
|----------------------------------------------|------------------------|----------------|------------|-----------|-------------------------|---------|
| Aging                                        | 0.492                  | 0.064          | 5.88       | 1.371     | 1.234~1.713              | 0.021   |
| Education level below college                | 0.32                   | 0.093          | 11.57      | 1.387     | 1.401~1.616              | 0.011   |
| BMI before pregnancy >26                     | 0.387                  | 0.087          | 10.167     | 1.306     | 1.334~1.698              | 0.007   |
| Body weight gain during pregnancy <40g per day| 0.333                  | 0.092          | 11.022     | 1.282     | 1.277~1.631              | 0.009   |
| Smoking                                      | 0.274                  | 0.091          | 12.34      | 1.401     | 1.356~1.701              | 0.009   |
| Drinking                                     | 0.314                  | 0.095          | 12.12      | 1.36      | 1.445~1.696              | 0.008   |
| No Vitamin D supplement                      | 0.413                  | 0.072          | 8.64       | 1.382     | 1.245~1.721              | 0.012   |
| Not consume milk products daily              | 0.331                  | 0.097          | 12.21      | 1.45      | 1.343~1.682              | 0.017   |

Correlations between vitamin D deficiency and adverse maternal and infant outcomes

Adverse maternal and infant outcomes, including preterm birth, adverse placental outcome, pre-eclampsia, gestational diabetes mellitus, gestational hypertension, placental abruption and intrauterine fetal death were recorded during follow-up. As shown in Table 3, vitamin D was significantly correlated with the occurrence of preterm birth, gestational diabetes mellitus, adverse placental outcome, pre-eclampsia and gestational hypertension (P<0.05), but not placental abruption and intrauterine fetal death.

Discussion

In this study, 23100 pregnant women were included, and 7526 females showed vitamin D deficiency, accounting for 32.58%, and 7649 females showed vitamin D inadequacy, accounting for 33.11%. Vitamin D deficiency during the second trimester of gestation (16 weeks) is common among non-manual workers in Shanghai, China according to IOM criteria (9). In Shanghai about 68.6% pregnant women were vitamin D deficient, and 21.9% were vitamin D inadequate (9). Those data suggest that vitamin D deficiency were significantly improved in pregnant women in Shanghai during the past 5 years. Latitude and season can significantly affect the production of vitamin D3 (11, 12). Areas greater than 35 degree latitude almost received no ultraviolet rays, which is important for the synthesis of vitamin D3. Shanghai is around 31 latitudes. However, high prevalence of vitamin D deficiency was observed, which is almost comparable to that of females in Taiyuan, China (35 degree latitude) (13). The high prevalence of vitamin D deficiency in Shanghai is possibly caused by factors other than high latitudes, such as air pollution, less physical activity and sedentary occupations (6).

Table 3: Correlation of serum vitamin D with maternal and infant outcomes

| Items                        | Cases | Deficiency (case, %) | Inadequacy (case, %) | Sufficiency (case, %) | χ²     | P value |
|------------------------------|-------|----------------------|----------------------|-----------------------|--------|---------|
| Preterm birth                |       |                      |                      |                       |        |         |
| Yes                          | 7963  | 2662                 | 2696                 | 2605                  | 13.718 | 0.001   |
| No                           | 15137 | 4864                 | 4953                 | 5320                  |        |         |
| Gestational diabetes mellitus|       |                      |                      |                       |        |         |
| Yes                          | 1344  | 477                  | 501                  | 366                   | 32.007 | P<.001  |
| No                           | 21756 | 7049                 | 7148                 | 7559                  |        |         |
| Pre-eclampsia                |       |                      |                      |                       |        |         |
| Yes                          | 2103  | 753                  | 751                  | 599                   | 34.984 | P<.001  |
| No                           | 20997 | 6773                 | 6898                 | 7326                  |        |         |
| Gestational hypertension     |       |                      |                      |                       |        |         |
| Yes                          | 1876  | 644                  | 653                  | 579                   | 10.747 | 0.005   |
| No                           | 21224 | 6882                 | 6996                 | 7346                  |        |         |
| Placental abruption          |       |                      |                      |                       |        |         |
| Yes                          | 464   | 155                  | 165                  | 144                   | 2.434  | 0.296   |
| No                           | 22636 | 7371                 | 7484                 | 7781                  |        |         |
| Intrauterine fetal death     |       |                      |                      |                       |        |         |
| Yes                          | 207   | 74                   | 75                   | 58                    | 3.665  | 0.160   |
| No                           | 22893 | 7452                 | 7574                 | 7867                  |        |         |

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Aging has been proven to be closely correlated with vitamin D deficiency among pregnant women. Vitamin D level in pregnant women younger than 20 years were significantly lower than those older than 20 years (14). Pregnant women younger than 20 years were not included in this study. However, our data showed that aging was closely correlated with vitamin D deficiency among pregnant women during the second trimester of gestation, and being older than 30 yr is an independent risk factor for this disease. Vitamin D deficiency is significantly more common among population without college education (15), which is consistent with the finding in our study that education level below colleges was an independent risk factor for vitamin D deficiency in second trimester of gestation. Milk is an important food resource of vitamin D, and maternal milk restriction during pregnancy can significantly reduce the intake of vitamin D (16). Consistently, our study also showed that not consume milk products daily can significantly increase the incidence of vitamin D deficiency. Conclusions on the effects of smoking, drinking, use of vitamin D supplement and ethnic backgrounds on vitamin D status are still controversial (13, 15). In our study, Being Han Chinese or minor group people showed no significant effect on vitamin D status, possibly due to the their similar lifestyle shaped by this rapidly developing city. However, smoking, drinking and no vitamin D supplement were proven to be independent risk factors for vitamin D deficiency. It is known that vitamin D status in human body depends on body mass index (BMI) (7). In our study, BMI before pregnancy >26 and body weight gain during pregnancy<40g/day were proved to be independent risk factors for vitamin D deficiency, further confirming the effects of BMI on vitamin D status. Vitamin D status affects not only health of mothers but also infant outcomes (17, 18). Maternal vitamin D deficiency may cause pro-inflammatory responses and increase oxidative reactions in mothers and fetus, leading to a serious of adverse event (19). Low maternal vitamin D levels in pregnancy may be associated with an increased risk of preeclampsia, gestational diabetes mellitus and preterm birth. In another study, insufficient vitamin D was at least partially responsible for the occurrence of gestational hypertension (20). Consistently, in this study, vitamin D was significantly correlated with the occurrence of preterm birth, gestational diabetes mellitus, pre-eclampsia and gestational hypertension. Placental abruption and intrauterine fetal death are two rare adverse pregnancy outcomes (21, 22). In this study, no significantly correlations were found between vitamin D status and the occurrences of placental abruption and intrauterine fetal death, which is inconsistent with another study (23), possibly due to the different ethnic background, different grouping method and the small sample size used in that study (n=227).

Conclusion

Vitamin D deficiency rate was significantly improved during past 5 years but still high among women in second trimester of pregnancy in Shanghai China. Vitamin D deficiency in second trimester of pregnancy was closely correlated with the occurrence of a serious of adverse maternal and infant outcomes, such as preterm birth, pre-eclampsia and gestational hypertension and gestational diabetes mellitus.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of Interest

The authors declare that there is no conflict of interests.

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