Association of Maternal Serum Vitamin D Level with Risk of Pregnancy-Related Complications and Neonatal Anthropometric Measures: A Prospective Observational Study

Abstract

Background: Body of evidence is increasing about the importance of Vitamin D (VD) for normal development of the fetus and for maternal health. As limited data are available regarding the association between maternal VD level and pregnancy-related complications and neonatal anthropometric measures, the present study aimed to evaluate the neonatal anthropometric measures including weight, high, and head circumference and pregnancy-related complications such as preeclampsia, blood pressure, gestational diabetes mellitus, and nausea and vomiting in pregnancy with 25(OH)VD level. **Methods:** The current prospective observational study was conducted among 812 Iranian pregnant women during the first trimester in Isfahan, Iran. Needed data were collected using validated questionnaires and biochemical examinations. **Results:** Overall, this study demonstrated an inverse significant association between VD level and chance of having low-weight infant in the adjusted model (odds ratio [OR]: 0.03, 95% confidence interval [CI]: 0.004–0.26, $P < 0.001$) in the first VD assessment. The same results were obtained in the second VD assessment (OR: 0.08, 95% CI: 0.01–0.40, $P < 0.01$). However, such associations were not seen about other neonatal measures and pregnancy-related complications. **Conclusions:** We found that low maternal VD level might be associated with risk of low-weight infant. Such findings could be considered to implement informative interventional programs to control newborn adverse outcomes. Further studies are required to confirm these findings.

Keywords: *Maternal Vitamin D, neonatal anthropometric measures, pregnancy complications*

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Introduction

Over the past three decades, it has become clear that the role of Vitamin D (VD) goes beyond the calcium homeostasis and bone health.[1-3] VD is involved in a wide range of physiological processes including the regulation of cell proliferation, differentiation, apoptosis and immune response, modification of the inflammatory pathways, and maintenance of genome stability function.[4-7]

Body of evidence is increasing about the importance of VD for normal development of the fetus and for maternal health.[8] During the early weeks of pregnancy, 1,25(OH)2D increases 2–3-fold despite minimal increased calcium demands during that time of gestation.[8] Furthermore, increased expression of VD receptor and its metabolic enzymes are reported at the placenta and decidua, indicating the potential role of

this nutrient on maternal and offspring outcomes.[4]

However, VD deficiency during pregnancy is prevalent among populations across the world.[8,9] VD deficient or insufficient, is common among those with avoidance of sun exposure to prevent melanoma, the use of sunscreen which blocks VD synthesis, traditional costumes that prevent people to expose themselves to sunlight and low dietary intake.[10,11]

VD deficiency may cause pregnancy-related complications such as preeclampsia and gestational diabetes leading to health threat for the mother and her infant.[4,8,9,12]

Furthermore, evidence links mentioned deficiency with adverse birth outcomes.[8,9] Neonatal anthropometric measures, including body weight (BW), head circumference (HC), and height (H), are widely assessed as parameters of impaired fetal growth, intrauterine environment, and

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How to cite this article: Hajianfar H, Esmaillzadeh A, Feizi A, Shahshahan Z, Azadbakht L. Association of maternal serum Vitamin D level with risk of pregnancy-related complications and neonatal anthropometric measures: A prospective observational study. Int J Prev Med 2019;10:208.

maternal nutrition.[13] Restriction fetal growth is traumatic and one of the most important global public health problems. It provides a foundation on which chronic disease may develop in offspring throughout their life.[14]

Several studies have reported a positive association between maternal VD levels in pregnancy and some neonatal outcomes[1] although results are inconsistent.[2,5] Such results were obtained about association of maternal VD status with pregnancy-related complications risk.[15] However, the effect of maternal VD deficiency on pregnancy-related complications and neonatal anthropometric measures is not clear.

As limited data are available regarding the association between maternal VD level and pregnancy-related complications and neonatal anthropometric measures in Middle Eastern countries where VD deficiency is prevalent,[16] the present study aimed to evaluate the neonatal anthropometric measures including weight, high, and HC and pregnancy-related complications such as preeclampsia, blood pressure (BP), gestational diabetes mellitus (GDM), and nausea and vomiting in pregnancy (NVP) with 25(OH) VD level. Such findings could be considered to implement informative interventional programs to control maternal and newborn adverse outcomes and develop practical policies to improve the diet quality among pregnant women.

Methods

Study design and participants

The current prospective observational study was conducted among 812 Iranian pregnant women during the first trimester to assess the relationship between 25(OH) VD level and neonatal anthropometric measures, including weight, high, and HC and pregnancy-related complications such as preeclampsia, BP, NVP, and GDM in Isfahan, Iran.

Eligible criteria included pregnant women during the 8–16 weeks of pregnancy without any medical condition, use of medications, and following a specific diet. Exclusion criteria were avoiding of follow-up and using of VD supplements during the study. The study population consisted of 812 pregnant women selected by the multistage cluster random sampling method. Sample size for this study was calculated statistics formula. Hence, according to this formula ($Z_{1-\alpha/2}$ = 1.96, $Z_{1-\beta}$ = 1.68, ∂^2 = R/6 = 100/6, and d = 3), 400 pregnant women were required for the study.

Informed consent was obtained from all participants. This study was approved by the research council (research project number: 193053) and ethics committee (research ethics number: IR.MUI.REC 193053).

Data collection

Assessment of Vitamin D level

At 8–16 weeks, maternal 25(OH)D level was analyzed by enzyme-linked immunosorbent assay method at the laboratory. The method measures total 25(OH)D (both 25(OH)D and D3). The second assessment was at 32–34 weeks. VD deficiency was defined conservatively as <10 ng/mL, insufficiency as 10–29 ng/mL, and sufficiency as >30 ng/mL.[17]

Assessment of pregnancy-related complications

Abnormal glucose homeostasis including fasting plasma glucose concentration >95 mg/dL and 1-h plasma glucose after eating 50 g of glucose >140 mg/dL at 24–28 gestational weeks was defined as GDM,[18] which assessed during the second visit at 24–28 weeks.

Preeclampsia is diagnosed in the presence of hypertension associated with proteinuria. Hypertension is defined as a BP of at least 140 mmHg (systolic) or at least 90 mmHg (diastolic) on at least two occasions and at least 4–6 h apart after the 20th week of gestation in women known to be normotensive beforehand. Proteinuria is also defined as a protein concentration of 300 mg/L or more in 24-h urine sample.[19]

BP was measured twice after the participants sat for 15 min during the first visit, at 8–16 weeks. A BP larger than systolic BP (SBP) ≥140 mmHg or diastolic BP (DBP) ≥90 mmHg during or after the 20th week of amenorrhea was considered as gestational hypertension.[20]

To assess NVP, participants were asked whether they had NVP during the first visit. Participants answered yes or no.

Assessment of growth measures of the newborn

Neonatal anthropometric measurements were performed by specially trained study personnel. All measurements including BW, HC, and height were recorded twice at birth and calculated as the mean of two measurements. Neonatal anthropometric measures were categorized according to the WHO standards and were as follows: low birth weight defines as the birth weight under 2500 g and normal birth weight also determines the birth weight from 2500 g to 3900, low height is the height less than 47 cm and normal height determines the height between (47-55) cm, low HC is the HC below 33 cm and normal HC is also the HC from 33 cm to 37 cm.[21]

Assessment of other variables

For the mothers, data were collected on the anthropometric measurements as well as demographic and clinical information.

To assess participants' information on age and gender, marital status, physical activity, educational, and socioeconomic levels, we used a standard self-reported questionnaire. Participants' weight was measured using a balanced scale digital scale to the nearest 100 g, in light clothing and barefoot. Height was measured with a tape measure while the participants were in a standing position. Body mass index (BMI), defined as weight in kilograms divided by height in meters squared, was calculated.[22]

Furthermore, energy and nutrient intakes were assessed by validated and reliable 117-item semi-quantitative food frequency questionnaire during the first visit, at 8–16 weeks. The validity and reliability of the questionnaire was previously confirmed.[23] For each item, participants were asked about the portion sizes and frequency of consumption in the previous year on a daily, weekly, or monthly basis. Portion sizes of consumed foods were converted to grams from household measures. We included supplements to total intake of specific nutrients. All nutrient values were energy adjusted using the residuals method. Then, nutrient and energy intakes were computed using Nutritionist IV software (version 7.0; N-Squared Computing, Salem, OR), which was designed for Iranian foods.

Statistical analysis

Data were statistically described in terms of mean ± standard deviation and percentages when appropriate. The results of Kolmogorov–Smirnov and Q-Q plot test and histogram showed that the distributions of quantitative variables were normal. Comparison of categorical variables between the study participants was done using Chi-square test. For comparing continuous variables, one-way analysis of variance was performed. Analysis of covariance was used for assessment of adjusted intakes of foods and nutrients across categories of VD levels including deficient, insufficient, and sufficient. Adjustments for energy intake, age and BMI, physical activity, and socioeconomic levels were considered in the adjusted model. All models were done by treating the deficient category of VD as the reference. $P < 0.05$ was considered statistically significant. All statistical calculations were done using computer programs SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 19 for Microsoft Windows.

Results

Pregnant women ($n = 812$), in their first trimester, consented to participate in this study. The overall characteristics of the study population across different categories of VD levels including deficient, insufficient, and sufficient are presented in Table 1.

Women with the sufficient levels of VD were more likely to be in the category of high economic level in both the first and the second VD assessment. In addition, they were significantly more likely to have low physical activity in the second VD assessment.

Crude and adjusted odds ratio (OR) and 95% confidence interval (CI) for ORs resulted from analysis, which neonatal anthropometric measures and pregnancy-related complications were as dependent variables and VD levels were as independent variables in different models, were given in Table 2. In all fitted models, the VD deficiency level was defined as the reference category.

The comparison of neonatal weight in different categories of VD levels showed VD sufficient levels which were related to neonatal weight in crude and adjusted model.

Women with VD sufficient level were less likely to having low-weight infant compared with those in the deficient level in crude (OR: 0.03, 95% CI: 0.004–0.23, $P < 0.001$) and in the adjusted model (OR: 0.03, 95% CI: 0.004–0.26, $P < 0.001$) in the first VD assessment. The same results were obtained in the second VD assessment in crude (OR: 0.09, 95% CI: 0.01–0.4, $P < 0.006$) and in the adjusted model (OR: 0.08, 95% CI: 0.01–0.40, $P < 0.01$).

However, VD sufficient level was not related height and HC of infants in all crude and adjusted models.

Finding about pregnancy-related complications showed that women in the different VD categories had not higher chance of having diabetes, intrauterine growth restriction, preeclampsia, SBP, DBP, BP, and NVP in the first and second assessment of VD.

Discussion

This study is one of the largest studies evaluating the association of maternal VD level during the first-trimester period of pregnancy with pregnancy-related complications and neonatal anthropometric measures. This study demonstrated an inverse significant association between VD level and chance of having low-weight infant. However, such associations were not seen about other neonatal measures and pregnancy-related complications.

The most important mechanism which may explain the association between 25(OH)D level and mentioned measures has been described such that VD regulates several genes throughout the body, as much as 5% of the human genome.[24] Earlier meta-analysis study has link VD deficiency with an increased risk of preeclampsia and GDM.[25] Furthermore, a significant correlation between VD with NVP was observed in early pregnancy.[26]

However, in a systematic review of observational studies, Harvey *et al*. identified inconsistent findings about the effect of maternal serum 25(OH)D concentration during pregnancy on gestational hypertension risk.[27]

About neonatal measures, consistent with this study, Leffelaar *et al*. showed that women with deficient VD levels had infants with lower birth weights compared with women with adequate VD levels.[28] Inconsistently, others found no independent relation between maternal VD levels and any of the neonatal anthropometric measures.[5]

We cannot rule out that the biological effect of VD could differ between the populations. The most important points that need to be considered are the genotypes coding for the VD receptor, VD binding protein, and regulatory enzymes which may all differ due to genetic background and be potential effect modifiers. Hence, it is more likely that this

Table 1: General characteristics of the study participants across different categories of Vitamin D in the first and third semester in pregnancy

	Vitamin D first				Vitamin D second			
	Deficiency	**Insufficient**	**Sufficient**	***P***	**Deficiency**	**Insufficient**	**Sufficient**	***P***
BMI								
Normal	79 (20)	223 (58)	77 (20)	<0.001	6 (21)	210 (73)	70 (24)	<0.001
Overweight	75 (24)	185 (59)	50 (16)		13 (5)	178 (72)	53 (21)	
Work mother								
Housekeeper	134 (24)	319 (59.1)	87 (16)	0.001	17 (3)	328 (75)	88 (20)	0.02
Employer	16 (14)	65 (59.1)	29 (26)		1 (1)	42 (60)	26 (37)	
Teacher	4 (11)	20 (58)	10 (29)		1 (4)	15 (62)	8 (33)	
Work husband								
Employer	47 (21)	113 (52)	54 (25)	0.001	4 (2)	102 (67)	45 (29)	0.002
Other	74 (19)	239 (64)	59 (15)		12 (4.1)	21 (71)	71 (24)	
Worker	32 (32)	55 (55)	12 (12)		2 (2)	75 (90)	6 (7)	
Education								
Diploma	72 (24)	181 (62)	36 (12)	0.03	11 (4)	188 (79)	37 (15)	0.001
Graduate	82 (20)	225 (56)	90 (22)		8 (2)	198 (67)	86 (29)	
Husband education								
Diploma	89 (25)	220 (61)	47 (13)	0.001	14 (4)	222 (79)	45 (16)	<0.001
Graduate	65 (19)	184 (55)	80 (24)		5 (2)	162 (66)	78 (31)	
Socioeconomic								
Low	11 (23)	32 (69)	3 (6)	0.02	3 (7)	34 (87)	2 (5)	0.003
Moderate	69 (27)	145 (57.1)	40 (15)		4 (2.1)	152 (78)	38 (19)	
High	65 (19)	193 (58)	73 (22)		8 (3)	171 (67)	73 (28)	
Delivery								
Cesarean	47 (19)	147 (60)	47 (19)		7 (4)	119 (68)	49 (28)	<0.001
Normal	107 (23)	261 (58)	79 (17)		12 (3)	269 (75)	73 (20)	
IUGR								
No	144 (22)	387 (59)	120 (18)	<0.001	18 (3)	360 (73)	115 (23)	<0.001
Yes	9 (27)	17 (51)	7 (21)		1 (3)	25 (78)	6 (18)	
Early delivery								
No	151 (22)	394 (58)	125 (18)	<0.001	19 (3)	377 (73)	118 (22)	<0.001
Yes	3 (20)	10 (66)	2 (13)		0	9 (75)	3 (25)	
Stillbirth								
No	153 (22)	404 (59)	125 (18)	<0.001	19 (3)	384 (73)	123 (23)	<0.001
Yes	1 (14)	4 (57)	2 (28)		0%	4 (100)	0	
Abortion								
No	123 (22)	326 (59)	98 (17)	<0.001	13 (3.1)	304 (72)	104 (24)	<0.001
Yes	31 (21)	82 (57)	29 (20)		6 (5)	84 (77.1)	19 (17)	
Activity								
Very low	2 (25)	4 (50)	2 (25)	0.01	0	3 (75)	1 (25)	<0.001
Low	88 (22)	216 (54)	93 (23)		12 (3)	217 (68)	88 (27)	
Moderate	52 (24.1)	143 (66)	21 (9)		6 (3)	134 (78)	30 (17)	
High	10 (17)	38 (64)	10 (17)		1 (3)	29 (87)	3 (9)	

BMI=Body mass index, IUGR=Intrauterine growth restriction

difference in results between studies is a result of residual genetic confounding.[29] We cannot also overlook the other confounding factors including the seasonal variation on VD level[30] as the study extended over a whole year. We also attribute this disparity in the results to the effects of maternal VD levels before placentation on maternal and newborn health outcomes.[31] Furthermore, assessment measurements error in results increase the likelihood of misclassification which contributes to the discrepancy among our results.

Another potential drawback should be also considered. Lack of funding to allow for more frequent examination to the whole study is an issue in the analyses. Hence, we did not identify a trend of VD level during pregnancy rather than a consistent level. In addition, women at higher risk of pregnancy-related complications were not excluded from the present study. Therefore, these potential limitations might be reasons why we failed to report significant associations between maternal VD

Table 2: The comparison of weight of neonatal, height of neonatal, head circumference of neonatal, and complication of pregnancy in different levels of Vitamin D in the first and third semester of pregnancy

	Vitamin D first				Vitamin D second			
	Deficiency	Insufficient	Sufficient	*P*	Deficiency	Insufficient	Sufficient	*P*
BMI								
Normal	79 (20)	223 (58)	77 (20)	<0.001	6 (21)	210 (73)	70 (24)	<0.001
Overweight	75 (24)	185 (59)	50 (16)		13 (5)	178 (72)	53 (21)	
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Housekeeper	134 (24)	319 (59.1)	87 (16)	0.001	17 (3)	328 (75)	88 (20)	0.02
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Other	74 (19)	239 (64)	59 (15)		12 (4.1)	21 (71)	71 (24)	
Worker	32 (32)	55 (55)	12 (12)		2 (2)	75 (90)	6 (7)	
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Graduate	82 (20)	225 (56)	90 (22)		8 (2)	198 (67)	86 (29)	
Husband education								
Diploma	89 (25)	220 (61)	47 (13)	0.001	14 (4)	222 (79)	45 (16)	<0.001
Graduate	65 (19)	184 (55)	80 (24)		5 (2)	162 (66)	78 (31)	
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Low	11 (23)	32 (69)	3 (6)	0.02	3 (7)	34 (87)	2 (5)	0.003
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No	153 (22)	404 (59)	125 (18)	<0.001	19 (3)	384 (73)	123 (23)	<0.001
Yes	1 (14)	4 (57)	2 (28)		0	4 (100)	0	
Abortion								
No	123 (22)	326 (59)	98 (17)	<0.001	13 (3.1)	304 (72)	104 (24)	<0.001
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High	10 (17)	38 (64)	10 (17)		1 (3)	29 (87)	3 (9)	

Resulted from ANCOVA. Adjusted Energy intake, age, physical activity, and socioeconomic levels. BMI=Body mass index, IUGR=Intrauterine growth restriction, ANCOVA=Analysis of covariance

level and pregnancy-related complications and neonatal anthropometric measures.

However, the main strengths of the current study include its multidisciplinary scope including epidemiology, statistics, pediatrics, maternity, and VD. Another positive point is that few studies have assessed the maternal VD levels on gestational complications and newborn measures.

Conclusions

In summary, evaluations carried out in the present study indicate an inverse significant association between maternal VD level and chance of having low-weight infant. Such findings could be considered to implement informative interventional programs to control newborn weight. Further studies are required to confirm these findings.

References

1. Wang H, Xiao Y, Zhang L, Gao Q. Maternal early pregnancy Vitamin D status in relation to low birth weight and small-for-gestational-age offspring. J Steroid Biochem Mol Biol 2018;175:146-50.

2. Lee CL, Ng BK, Wu LL, Cheah FC, Othman H, Ismail NA, *et al.* Vitamin D deficiency in pregnancy at term: Risk factors and pregnancy outcomes. Horm Mol Biol Clin Investig 2017;31. pii:/j/hmbci. 2017.31.

3. Schulz EV, Cruze L, Wei W, Gehris J, Wagner CL. Maternal Vitamin D sufficiency and reduced placental gene expression in angiogenic biomarkers related to comorbidities of pregnancy. J Steroid Biochem Mol Biol 2017;173:273-9.

4. Ji JL, Muyayalo KP, Zhang YH, Hu XH, Liao AH. Immunological function of Vitamin D during human pregnancy. Am J Reprod Immunol 2017;78. doi: 10.1111/aji.12716.

5. Eggemoen ÅR, Jenum AK, Mdala I, Knutsen KV, Lagerløv P, Sletner L, *et al.* Vitamin D levels during pregnancy and associations with birth weight and body composition of the newborn: A longitudinal multiethnic population-based study. Br J Nutr 2017;117:985-93.

6. Silva-Zolezzi I, Samuel TM, Spieldenner J. Maternal nutrition: Opportunities in the prevention of gestational diabetes. Nutr Rev 2017;75:32-50.

7. Gbadegesin A, Sobande A, Adedeji O, Disu E, Korede O, Dosunmu A, *et al.* Maternal serum Vitamin D levels and pregnancy outcomes: From lagos, Nigeria. J Obstet Gynaecol 2017;37:25-8.

8. Wagner CL, Hollis BW, Kotsa K, Fakhoury H, Karras SN. Vitamin D administration during pregnancy as prevention for pregnancy, neonatal and postnatal complications. Rev Endocr Metab Disord 2017;18:307-22.

9. Naseh A, Ashrafzadeh S, Rassi S. Prevalence of Vitamin D deficiency in pregnant mothers in tehran and investigating its association with serum glucose and insulin. J Matern Fetal Neonatal Med 2017;31:2312-8.

10. Haham M, Ish-Shalom S, Nodelman M, Duek I, Segal E, Kustanovich M, *et al.* Stability and bioavailability of Vitamin D nanoencapsulated in casein micelles. Food Funct 2012;3:737-44.

11. Mohammadi M, Ghanbarzadeh B, Hamishehkar H. Formulation of nanoliposomal Vitamin D3 for potential application in beverage fortification. Adv Pharm Bull 2014;4:569-75.

12. Brown J, Ceysens G, Boulvain M. Exercise for pregnant women with gestational diabetes for improving maternal and fetal outcomes. Cochrane Database Syst Rev 2017;6:CD012202.

13. Zhang YQ, Li H. Changes in weight, length, head circumference, and ponderal index at birth of healthy term newborns in nine cities in China during the period of rapid social development 1985-2005. Econ Hum Biol 2015;19:45-50.

14. Iheozor-Ejiofor Z, Middleton P, Esposito M, Glenny AM. Treating periodontal disease for preventing adverse birth outcomes in pregnant women. Cochrane Database Syst Rev 2017;6:CD005297.

15. De-Regil LM, Palacios C, Lombardo LK, Peña-Rosas JP. Vitamin D supplementation for women during pregnancy. Cochrane Database Syst Rev 2016;14:CD008873. doi: 10.1002/14651858.CD008873.

16. Hovsepian S, Amini M, Aminorroaya A, Amini P, Iraj B. Prevalence of Vitamin D deficiency among adult population of Isfahan city, Iran. J Health Popul Nutr 2011;29:149-55.

17. Abedi P, Mohaghegh Z, Afshary P, Latifi M. The relationship of serum Vitamin D with pre-eclampsia in the Iranian women. Matern Child Nutr 2014;10:206-12.

18. Mahan LK, Escott-Stump S, Krause MV. Krause's Food & Nutrition Therapy. 12th ed. Philadelphia, PA; Edinburgh: Elsevier Saunders, 2008.

19. Cunningham F, Leveno K, Bloom S, Spong CY, Dashe J. Williams Obstetrics, 24th ed. Amazon: Mcgraw-Hill; 2014.

20. Fauvel JP. Hypertension during pregnancy: Epidemiology, definition. Presse Med 2016;45:618-21.

21. World Health Organiziation. Anthropometric Reference Data for International Use. Available from: http://www.who.int/childgrowth/en/2017/12/01. [Last accessed on 2019 Sep 23].

22. Miraghajani M, Zaghian N, Mirlohi M, Feizi A, Ghiasvand R. The impact of probiotic soy milk consumption on oxidative stress among type 2 diabetic kidney disease patients: A Randomized controlled clinical trial. J Ren Nutr 2017;27:317-24.

23. Hashemi R, Motlagh AD, Heshmat R, Esmaillzadeh A, Payab M, Yousefinia M, *et al.* Diet and its relationship to sarcopenia in community dwelling Iranian elderly: A cross sectional study. Nutrition 2015;31:97-104.

24. Aghajafari F, Nagulesapillai T, Ronksley PE, Tough SC, O'Beirne M, Rabi DM, *et al.* Association between maternal serum 25-hydroxyvitamin D level and pregnancy and neonatal outcomes: Systematic review and meta-analysis of observational studies. BMJ 2013;346:f1169.

25. Wei SQ, Qi HP, Luo ZC, Fraser WD. Maternal Vitamin D status and adverse pregnancy outcomes: A systematic review and meta-analysis. J Matern Fetal Neonatal Med 2013;26:889-99.

26. Jwa SC, Ogawa K, Kobayashi M, Morisaki N, Sago H, Fujiwara T, *et al.* Validation of a food-frequency questionnaire for assessing vitamin intake of Japanese women in early and late pregnancy with and without nausea and vomiting. J Nutr Sci 2016;5:e27.

27. Harvey NC, Holroyd C, Ntani G, Javaid K, Cooper P, Moon R, *et al.* Vitamin D supplementation in pregnancy: A systematic review. Health Technol Assess 2014;18:1-90.

28. Leffelaar ER, Vrijkotte TG, van Eijsden M. Maternal early pregnancy Vitamin D status in relation to fetal and neonatal growth: Results of the multi-ethnic amsterdam born children and their development cohort. Br J Nutr 2010;104:108-17.

29. Eggemoen ÅR, Jenum AK, Mdala I, Knutsen KV, Lagerløv P, Sletner L, *et al.* Vitamin D levels during pregnancy and associations with birth weight and body composition of the newborn: A longitudinal multiethnic population-based study. Br J Nutr 2017;117:985-93.

30. Lips P. Vitamin D status and nutrition in Europe and Asia. J Steroid Biochem Mol Biol 2007;103:620-5.

31. Wagner CL, Hollis BW, Kotsa K, Fakhoury H, Karras SN. Vitamin D administration during pregnancy as prevention for pregnancy, neonatal and postnatal complications. Rev Endocr Metab Disord 2017;18:307-22.