Original Article

High Prevalence of Vitamin D Deficiency and Adverse Pregnancy Outcomes in Yazd, a Central Province of Iran

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Abstract

Background: There is a growing concern about the high prevalence of vitamin D deficiency and its relationship with variety of diseases worldwide. The objective of this study was to determine the prevalence of vitamin D deficiency and its relationship with pregnancy adverse effects in Yazd.

Methods: This was a cross sectional study conducted among 200 nulliparous women from October 2013 to April 2014. Data containing socio-demographic and personal details, vitamin D level, pregnancy complications and growth situation of newborns were collected and analyzed using Mann-Whitney, Kruskal-Wallis and Pearson's correlation coefficient by SPSS. $p<0.05$ was considered statistically significant.

Results: The mean serum 1, 25 $(OH)_2D_3$ concentration was 20.3±10.8 $\mu g/l$. Totally, 78% of the women had less than sufficient levels. Mean of vitamin D was significantly higher in natural or elective cesarean in comparison with abortion and emergency cesarean (p=0.040). Risk of abortion was 3.1(1.39-6.8) and higher in severely deficient group in comparison to women with vitamin D deficiency (p=0.017) and mean of vitamin D group was significantly lower in women who had oligohydramnios or polyhydramnios complication (p=0.045).

Conclusion: The study findings revealed that vitamin D deficiency is prevalent in pregnant women and it is significantly associated with elevated risk for abortion, and oligohydramnios or polyhydramnios. Probably, a targeted screening strategy can be suggested to detect and treat women at high risk of vitamin D deficiency in early pregnancy as a simple way to reduce the risk of these adverse pregnancy outcomes in Yazd.

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Introduction

Humans receive vitamin D from exposure to sunlight, diet and dietary supplements. The skin synthesis of vitamin D induced by ultraviolet B radiation is the main determinant of vitamin D status in the population because few food items contain or are fortified with vitamin D (1). Vitamin D status is a well-known determinant of bone health and correlated with a risk of many diseases such as cancers (2), cardiovascular diseases (3), diabetes (4), *etc*. There is a growing concern about the effects of the high prevalence of vitamin D deficiency worldwide in general population, including pregnant women (5). Important modifications occur in the calcium metabolism and maternal concentration of vitamin D during pregnancy. Calcium is transported from the mother to the fetus through the placenta (6). However, vitamin D deficiency during pregnancy is related with the actions of this hormone, being linked with preeclampsia insulin resistance, and gesta-

tional diabetes mellitus (7-9). Notably, vitamin D deficiency prevalence is 20-85% during pregnancy, depending on country of residence and other related factors (10, 11).

In developing countries, 18% of global burden of diseases has been related to pregnancy complications (12). The prevalence of vitamin D deficiency has been an important issue in both developing and developed countries in recent years (13, 14). Wearing concealing cloth in women in some countries such as India (15), Saudi Arabia (16), and Iran (17), because of their cultures, and United Kingdom (18) and Norway (19) in northern latitudes with cold weather has been the main reason for high risk of vitamin D deficiency.

In a review, it was advised that women with risk factors for low serum 1, 25 $(OH)_2D_3$ should be monitored at the beginning and middle of pregnancy (20).

At present, there is not enough evidence to assess the vitamin D status and relationship with adverse effects in pregnancy in Yazd as a central province in Iran. So, the objective of this study was to determine the prevalence of vitamin D deficiency and its relationship with pregnancy's adverse effects. Therefore, describing current situation can be used as a guideline for deciding to include determining the level of vitamin D as one of the routine tests in early pregnancy and appropriate interventions in order to raise the health of these pregnant women in future planning and decision making.

Methods

This was a cross sectional study conducted among 200 pregnant women on the verge of giving birth who were admitted in Shahid Sadoughi hospital delivery room for termination of pregnancy from October 2013 to April 2014 in Yazd, Iran. The women were selected according to a non proportionate sampling. Participants were the nulliparous women who were supposed to undergo one of the processes included in natural delivery, elective or emergency cesarean section and abortion. Women with a history of any underlying problem and medications influencing calcium or vitamin D metabolism including renal and bone disorders were excluded.

A general questionnaire about socio-demographic and personal details (age, education, job, gestational age, gestational rank, delivery type), regular use of multivitamins during the current pregnancy and complications (preeclampsia, gestational diabetes, polyhydramnios, oligohydramnios, abortion, premature rupture of membrane (PROM)) during pregnancy, and neonatal situation containing APGAR score and growth index of neonates *e.g.* weight, height and head circumference, was completed in a face-to-face interview and reading their documents conducted by the study nurse.

Approximately, 5 *ml* of whole blood was collected by venipuncture in a non-heparinized tube. The clotted blood was centrifuged and serum samples were stored at -80°*C* until use. Serum concentration of 1, 25 $(OH)_2D_3$ was determined using an enzyme-linked immunosorbent assay (ELISA) kit following the manufacturer's instructions. For the analysis, in our study, women were classified into groups that defined vitamin D status: severe vitamin D deficiency: 1, 25 $(OH)_2D_3$<10 *μg/l*; vitamin D deficiency: 10-20 *μg/l*; vitamin D insufficiency: 20-30 *μg/l*; vitamin D sufficiency: 1, 25 $(OH)_2D_3$30-50 *μg/l*. Vitamin D upper normal or toxic: 1, 25 $(OH)_2D_3$>50 *μg/l* (21).

Data were analyzed using SPSS version 20. Mann-Whitney and Kruskal-Wallis were used to ascertain the significance of differences between mean values of two continuous non normal distributed variables. Pearson's correlation coefficient was used to evaluate the strength association between two continuous variables after normalizing distributions using logarithm of these variables. All statistical tests were two-sided, and $p< 0.05$ was considered statistically significant. This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the medical ethical committee of the Shahid Sadughi Medical Sciences University in Yazd. The subjects provided written consent for participation in the study.

Results

The mean age of participants was 26.74±6.3 years (range 15-47 years). Of all pregnant women included, 51.3% (102) were less than diploma and, and 48.7% (98) diploma and more university educated, 97.5% (194) were housewives and 2.5% (6) had another job. Among them, 48.8% (97) had natural delivery, 29.9% (60) elective cesarean, 15.9% (32) emergency cesarean and 5.5% (11) abortion. 38.5% (77) of pregnant women were taking multivitamins containing vitamin D during pregnancy, and 61.5% (123) didn't use any supplement.

The mean serum 1, 25 $(OH)_2D_3$ concentration of

Table 1. The means of using vitamin D according to demographic factors and pregnancy complications in pregnant women

Variables	Vitamin D M±SD	P-value
Education		0.2 *
Less than diploma	19.6±10.7	
Diploma and more	21.3±10.9	
Job		0.3 *
Housewives	20.5±10.8	
Employed	14.6±2.4	
Type of delivery		0.04 **
Natural	20.4±10.9	
Elective cesarean	22.2±9.2	
Emergency cesarean	16.3±7.5	
Abortion	17.2±14.6	

*Mann-Whitney; **Kruskal-Wallis

Table 2. The means of using vitamin D according to having varieties of pregnancy complications or not in pregnant women

Complications	Vitamin D M±SD	P-value
Preeclampsia		0.87*
no	20.2±10.6	
yes	21.7±13.1	
PROM		0.36*
no	20.3±10.9	
yes	22.1±7.7	
Pregnancy diabetes		0.32*
no	20.3±11.1	
yes	21.2±8.4	
Oligohydramnios or Polyhydramnios		0.045*
no	20.6±10.8	
yes	13.9±9.5	

*Mann-Whitney

women (n=200) was 20.3±10.8 (range 4.5-51.2) *μg/l*. Totally, 18% of women had sufficient serum 1, 25 $(OH)_2D_3$ concentrations and 78% and 4% had less than sufficient and upper normal or toxic levels, respectively.

Generally, 66% (132) of women had no problem during pregnancy, whereas 9.5% (19) experienced preeclampsia, 6.5% (13) premature rupture of membrane, 9% (18) gestational diabetes, 3% (6) oligohydramnios, 0.5% (1) polyhydramnios and 5.5% (11) abortion. Among different demographic or personal variables and various complications, mean of vitamin D was significantly higher in natural or elective cesarean in comparison with abortion and emergency cesarean in those pregnant women (p=0.040). Furthermore, risk of abortion was 3.1 (1.39-6.8) and higher in severe deficiency group in comparison with vitamin D deficiency group (p=0.017). Mean of vitamin D was significantly lower in women who had oligohydramnios or polyhydramnios complication (p=0.045). Description for other factors has been shown in tables 2 and 3 (Tables 1 and 2). The mean birth weight of newborns of mothers with vitamin D deficiency was 3128±415 *gr* in comparison with 3132±372 *gr* in mothers with sufficient vitamin D (p=0.9), and correlations between other neonatal growth status of pregnant women and vitamin D level of these mothers were not statistically significant (Table 3).

Table 3. Correlation between neonatal growth status and vitamin D levels in pregnant women

Logarithm of neonatal growth status variables	Pearson correlation(r)	P-value
Birth weight	0.05	0.5
Birth height	0.04	0.6
Head circumference	0.02	0.7
APGAR at first minute	0.04	0.6
APGAR at fifth minute	0.03	0.7

Discussion

Despite the fact that nearly 40% of the pregnant women reported taking multivitamins containing vitamin D during pregnancy, almost 60% of the women were vitamin D deficient, among them 12.5% were severely deficient. This was similar to previous studies in Yazd (22) and other provinces of Iran that totally reported 64 to 75% of vitamin D deficiency in pregnant women (23-25).

Other studies have demonstrated that vitamin D deficiency is common in pregnant women in different countries, such as 31% in southern India (15), 19.5% in Greece (26) and 96.8% in china (27). Considering the diversity of factors which affect vitamin D level in different countries including sunshine exposure, wearing habits, diet, season of study, variation of vitamin D deficiency prevalence is expected. But it is notable that the place of our study (Yazd) is located in a desert and it is sunny most of the days and living in apartment is not as common as other provinces of Iran. So maybe clothing habits, harmful effects of sun on skin and unawareness of the necessity of sunlight for synthesizing vitamin D are the most affecting factors which determine vitamin D levels in women.

The present study demonstrated a greater risk of abortion and oligohydramnios or polyhydramnios among maternal complications assessed in pregnant women with vitamin D deficiency compared with those with normal vitamin D levels. In one *in vitro* study, the results indicated the potential beneficial effects of vitamin D in patients with URSA (unexplained recurrent spontaneous abortion) (28) and another study promoted the use of vitamin D as a new immunomodulatory agent in treatment of recurrent spontaneous abortion considering immunosuppressive effect of vitamin D (29).

However, no statically significant relationship was found between vitamin D deficiency and other pregnancy problems unlike other studies which reported various results in case of relationship between pregnancy problems and vitamin D deficiency (30-32).

In contrast to several studies which didn't find any statically significant correlation between growth situation of neonates and the levels of vitamin D in mothers (33, 34), our findings were similar to a report of one study done in UK which concluded that there were no associations between maternal 1, 25 $(OH)_2D_3$ concentrations and the child's outcomes including body size at birth (18).

These findings provide evidence suggesting that vitamin D deficiency or insufficiency is common during pregnancy, which leads to some adverse pregnancy outcomes such as abortion, oligohydramnios or polyhydramnios.

However, some limitations in our study can be observed; firstly, assessing vitamin D deficiency in all seasons could be more useful instead of just two seasons in this study and secondly more complete results could be achieved by checking other complications detected in paraclinic services for participants, such as sonography, blood test and urine exam. Thirdly, given that oligohydramnios and polyhydramnios are correlated to preeclampsia and gestational diabetes, respectively, they could not be analyzed in subgroups properly, because of inadequate sample size.

Conclusion

In conclusion, the study findings revealed that vitamin D deficiency is prevalent in pregnant women and it is significantly associated with elevated risk for abortion, and oligohydramnios or polyhydramnios.

Probably, a targeted screening strategy to detect and treat women at high risk of vitamin D deficiency might be useful in Yazd and maybe in other provinces of Iran. While several observational studies point to correlations between vitamin D insufficiency and other maternal and neonatal adverse outcomes, experimental evidence from clinical trials is needed to inform policy makers.

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Conflict of Interest

The study was funded by the Monitoring Health Research Centre at Shahid Sadughi University of Medical Science; Grant number: 1027.

The authors declare that they have no conflict of interests.

References

1. Holick MF. Vitamin D deficiency. N Engl J Med. 2007;357(3):266-81.
2. Lappe JM, Travers-Gustafson D, Davies KM, Recker RR, Heaney RP. Vitamin D and calcium supplementation reduces cancer risk: results of a randomized trial. Am J Clin Nutr. 2007;85(6):1586-91.
3. Semba RD, Houston DK, Bandinelli S, Sun K, Cherubini A, Cappola AR, et al. Relationship of 25-hydroxyvitamin D with all-cause and cardiovascular disease mortality in older community-dwelling adults. Eur J Clin Nutr. 2010;64(2):203-9.
4. Martini LA, Wood RJ. Vitamin D status and the metabolic syndrome. Nutr Rev. 2006;64(11):479-86.
5. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011;96(7):1911-30.
6. Shin JS, Choi MY, Longtine MS, Nelson DM. Vitamin D effects on pregnancy and the placenta. Placenta. 2010;31(12):1027-34.
7. Lapillonne A. Vitamin D deficiency during pregnancy may impair maternal and fetal outcomes. Med Hypotheses. 2010;74(1):71-5.
8. Haugen M, Brantsaeter AL, Trogstad L, Alexander J, Roth C, Magnus P, et al. Vitamin D supplementation and reduced risk of preeclampsia in nulliparous women. Epidemiology. 2009;20(5):720-6.
9. von Hurst PR, Stonehouse W, Coad J. Vitamin D supplementation reduces insulin resistance in South Asian women living in New Zealand who are insulin resistant and vitamin D deficient - a randomised, placebo-controlled trial. Br J Nutr. 2010;103(4):549-55.

10. Mulligan ML, Felton SK, Riek AE, Bernal-Mizrachi C. Implications of vitamin D deficiency in pregnancy and lactation. Am J Obstet Gynecol. 2010;202(5):429.e1-9.
11. Bodnar LM, Simhan HN, Powers RW, Frank MP, Cooperstein E, Roberts JM. High prevalence of vitamin D insufficiency in black and white pregnant women residing in the northern United States and their neonates. J Nutr. 2007;137(2):447-52.
12. AbouZahr C. Global burden of maternal death and disability. Br Med Bull. 2003;67:1-11.
13. Dawodu A, Akinbi H. Vitamin D nutrition in pregnancy: current opinion. Int J Womens Health. 2013;5:333-43.
14. Viljakainen HT, Saarnio E, Hytinantti T, Miettinen M, Surcel H, Makitie O, et al. Maternal vitamin D status determines bone variables in the newborn. J Clin Endocrinol Metab. 2010;95(4):1749-57.
15. Sahu M, Bhatia V, Aggarwal A, Rawat V, Saxena P, Pandey A, et al. Vitamin D deficiency in rural girls and pregnant women despite abundant sunshine in northern India. Clin Endocrinol (Oxf). 2009;70(5):680-4.
16. Aly YF, El Koumi MA, Abd El Rahman RN. Impact of maternal vitamin D status during pregnancy on the prevalence of neonatal vitamin D deficiency. Pediatr Rep. 2013;5(1):e6.
17. Salek M, Hashemipour M, Aminorroaya A, Gheiratmand A, Kelishadi R, Ardestani PM, et al. Vitamin D deficiency among pregnant women and their newborns in Isfahan, Iran. Exp Clin Endocrinol Diabetes. 2008;116(6):352-6.
18. Gale CR, Robinson SM, Harvey NC, Javaid MK, Jiang B, Martyn CN, et al. Maternal vitamin D status during pregnancy and child outcomes. Eur J Clin Nutr. 2008;62(1):68-77.
19. Madar AA, Stene LC, Meyer HE. Vitamin D status among immigrant mothers from Pakistan, Turkey and Somalia and their infants attending child health clinics in Norway. Br J Nutr. 2009;101(7):1052-8.
20. Camadoo L, Tibbott R, Isaza F. Maternal vitamin D deficiency associated with neonatal hypocalcaemic convulsions. Nutr J. 2007;6:23.
21. Bouillon R, Van Schoor NM, Gielen E, Boonen S. Optimal vitamin D status: a critical analysis on the basis of evidence-based medicine. J Clin Endocrinol Metab. 2013;98(8):1283-304.
22. Shakiba M, Rafiei P. Prevalence of vitamin D deficiency among medical staff in Shahid Sadoughi Hospital in Yazd, Iran. Tolloebehdasht. 2008;7(3-4):22-30.
23. Moussavi M, Heidarpour R, Aminorroaya A, Pournaghshband Z, Amini M. Prevalence of vitamin D deficiency in Isfahani high school students in 2004. Horm Res. 2005;64(3):144-8.
24. Rahimi AO, Zarghami N, Sadighi A. Relationship between vitamin D and nutritional status in healthy reproductive age women. Int J Endocrinol Metab. 2006;4(1):1-7.
25. Moradzadeh K, Larijani B, Keshtkar A, Hossein-Nezhad A, Rajabian R, Nabipour I, et al. Normative values of vitamin D among Iranian population: a population based study. Int J Osteoporos Metab Disord. 2008;1(1):8-15.
26. Nicolaidou P, Hatzistamatiou Z, Papadopoulou A, Kaleyias J, Floropoulou E, Lagona E, et al. Low vitamin D status in mother-newborn pairs in Greece. Calcif Tissue Int. 2006;78(6):337-42.
27. Song SJ, Zhou L, Si S, Liu J, Zhou J, Feng K, et al. The high prevalence of vitamin D deficiency and its related maternal factors in pregnant women in Beijing. PLoS One. 2013;8(12):e85081.
28. Tavakoli M, Jeddi-Tehrani M, Salek-Moghaddam A, Rajaei S, Mohammadzadeh A, Sheikhhasani S, et al. Effects of 1,25(OH)2 vitamin D3 on cytokine production by endometrial cells of women with recurrent spontaneous abortion. Fertil Steril. 2011; 96(3):751-7.
29. Bubanovic I. 1alpha,25-dihydroxy-vitamin-D3 as new immunotherapy in treatment of recurrent spontaneous abortion. Med Hypotheses. 2004;63 (2):250-3.
30. Shand AW, Nassar N, Von Dadelszen P, Innis SM, Green TJ. Maternal vitamin D status in pregnancy and adverse pregnancy outcomes in a group at high risk for pre-eclampsia. BJOG. 2010;117(13):1593-8.
31. Aghajafari F, Nagulesapillai T, Ronksley PE, Tough SC, O'Beirne M, Rabi DM. 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.
32. Soheilykhah S, Mojibian M, Rashidi M, Rahimi-Saghand S, Jafari F. Maternal vitamin D status in gestational diabetes mellitus. Nutr Clin Pract. 2010;25(5):524-7.
33. Mannion CA, Gray-Donald K, Koski KG. Association of low intake of milk and vitamin D during pregnancy with decreased birth weight. CMAJ. 2006;174(9):1273-7.
34. 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(1):108-17.