Examining Vitamin D Level at the End of First Trimester and its Relation with Anemia, Bacterial Vaginosis, and Toothache in Pregnant Mothers Referred to Isfahan Beheshti and Al-Zahra Hospitals in 2012-2013

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Abstract: Introduction: The need for vitamin D is higher at certain stages of life. These stages include embryonic period, infancy, early childhood, puberty, pregnancy and lactation. During pregnancy, calcium absorption increases through the digestive tube and with high concentration of vitamin D. During pregnancy, vitamin D increases HPL-HCG, estrogen and progesterone in matured placenta, and its deficiency during pregnancy increases preeclampsia, gestational diabetes, toothache, anemia and bacterial vaginosis in mother, and may cause postpartum seizures, PTL, SGA, IUGR, osteomalacia, infantile rickets, and craniotabes in new-born infants. This study conducted to evaluate Vitamin D Level at the End of First Trimester and its Relation with Anemia, Bacterial Vaginosis, and Toothache in Pregnant Mothers in Isfahan.

Materials and Methods: this cross-sectional study with a developmental plan has been conducted in the first trimester of pregnancy (week 12) on the women referred to Shariati and Al-Zahra Teaching Hospitals in 2012-2013. The study was done in a range of one year and 280 individuals were selected after statistical calculation. Simple sampling method was used and for each sample Vit D (OH) 125 serum level was measured using E-lex's and Electrochemi-luminescence method (ECLIA) and more information were collected through questionnaire and analysed in the survey. All data were stored in SPSS software and then analysed using t-test and X2 tests.

Results: vitamin D level in 280 pregnant women ranged from 1 to 80. Vitamin D deficiency was examined in four groups of severe deficiency (0-20), moderate deficiency (20-40), mild deficiency (40-60) and normal (higher than 60), and a significant relationship was observed between vitamin D level and associated factors.

Conclusion: In this study, anemia, bacterial vaginosis and toothache were more observed in the mothers with low levels of vitamin D.

Keywords: Vitamin D, Anemia, Bacterial vaginosis, Pregnancy

1. Introduction

Pregnancy is associated with significant changes in calcium metabolism and the basic function of these changes is to provide adequate calcium for fetal skeletal growth and mineralization. In other words, the need for vitamin D is higher at certain stages of life. These stages include embryonic period, infancy, early childhood, puberty, pregnancy and lactation in which, vitamin D deficiency is more

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obvious (Sabour H.2004).During pregnancy, calcium absorption increases through the digestive tube and with high concentration of vitamin D. During pregnancy, vitamin D increases HPL-HCG, estrogen and progesterone in matured placenta (Heaney Rp,2003), and its deficiency during pregnancy increases preeclampsia, gestational diabetes, toothache, anemia and bacterial vaginosis in mother, and may cause postpartum seizures, PTL, SGA, IUGR, osteomalacia, infantile rickets, and craniotabes in newborn infants(William B,2011,Zare'an E,2012).

An increase of Vit D (OH) 125 in first trimester will increases calcium absorption and homeostasis; in fact vitamin D functions as placental calcium transport regulator (Bruns ME,1983). Perhaps the most important effect of vitamin D returns to its innate ability in enhancing immune responses, especially its anti-microbial activity (Adamsy S, 2007).Therefore, according to these problems, determining vitamin D level during pregnancy and its treatment may help to prevent many maternal and neonatal complications. Several studies show that the clinical and subclinical prevalence of vitamin D deficiency is increased during pregnancy since the fetus is directly dependent on maternal vitamin D stores (Groves SR,2012).

In placenta and pregnancy tissues a wide range of anti-bacterial and anti-viral factors are produced. It seems that high levels of vitamin D local production in placenta can affect these anti-microbial factors (Zare'an E,2012). In Vitro studies have shown that vitamin D can cause cathelicidin of antibacterial protein in maternal deciduas and fetal trophoblast (Laskarin G,2007). Vitamin D deficiency increases the incidence of bacterial vaginosis in the first trimester of pregnancy (Adamsy S, 2007). Studies on cultured deciduas cells have shown that treatment by vitamin D can cause a range of cytokines and lead to inhibition of placental inflammation (Lip PT, 2006).

The prevalence of anemia among the pregnant women is considerable. Studies have shown that there is a significant relationship between vitamin D deficiency and anemia so that vitamin D deficiency causes 12% anemia during the first trimester and 50% anemia during the third trimester of pregnancy. In other studies, up to 81.6% anemia has been reported during pregnancy. The prevalence of anemia in the first, second and third trimesters, has respectively been as 10.3, 13.5 and 12.7 percent (Davari F,2004). Vitamin D also increases calcium absorption in teeth. In this regard, according to the studies, the incidence of toothache in people with vitamin D deficiency has been reported to be approximately 2 percent (With, 2008).

Given the role of vitamin D and multiple complications in pregnancy caused by vitamin D deficiency, it should be noted that vitamin D deficiency, as one of the essential micronutrients, can lead to anemia, bacterial vaginosis and toothache, sothis study conducted with aim of determining vitamin D level in the first trimester of pregnancy and its relation with anemia, bacterial vaginosis and toothache were examined in pregnant women referred to Shariati and Al-Zahra Teaching Hospitals.

Materials and Methods

This cross-sectional study has been conducted in the first trimester of pregnancy (week 12) on the women referred to Shariati and Al-Zahra Teaching Hospitals in 2012-2013. The study was done in a range of one year and 280 individuals were selected after statistical calculation. In this study, through convenient sampling method and taking blood samples, vitamin D level was tested in the pregnant women who were in their first trimester. Samples were taken from the patients and following testing standards, tests were performed in laboratory. Vitamin D level was measured using E-lex's and Electrochemi-luminescence method (ECLIA), and then, the laboratory estimated level of vitamin D was determined in four groups: severe deficiency (0-20 nm/dlit), moderate deficiency (20-40), mild deficiency (40-60) and normal (higher than 60). Moreover, information related to supplements received by the mothers, general situation of health, use of medicine during pregnancy, pre-pregnancy weight, first trimester weight, maternal age, place of living, receiving vitamin D, maternal hemoglobin level, bacterial vaginosis infection, and toothache in the first trimester were collected through questionnaire and analyzed in the survey. All data were stored

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in SPSS software and then analyzed using t-test and X2 tests.

Inclusion criteria: all pregnant women referred to prenatal clinic with 1-4 parity, being in the first trimester, having no chronic or disabling disease, no use of supplements or medications that may interfere with in vitro vitamin D level. Informed consents were taken from all women before entering into the study.

Exclusion criteria: mothers' dissatisfaction with the test, taking any supplement and medication which affects in vitro level of vitamin D, any chronic and disabling disease in mother, and other underlying diseases which may affect maternal hb and vitamin D level.

Descriptive statistics include frequency distribution tables, and obtained mean and standard deviations. In inferential statistic part, Chi-square, Fisher exact test, Mann-Whitney test, independent t-test, and Pearson and Spearman correlation coefficient were used.

Findings and Results:

In this study, 280 mothers were examined whose characteristics were as follows: mothers aged between 18 and 38 years old with the mean of 26.2 ± 4.81. Frequency distribution of vitamin D deficiency was 80.3% (n=224) in severe deficiency group (0-20), 11.8% (n=33) in moderate deficiency group (20-40), 5.1% (n=14) in mild deficiency group, and 1.8% (n=5) in normal group. Distribution of vitamin D deficiency in the mothers in terms of their education level has been shown in table1. And also distribution of vitamin D deficiency in the mothers in terms of parity has been shown in table2.

Table1- Frequency distribution of vitamin D deficiency in the mothers in terms of their education

	Under diploma	Diploma	Associate degree	Bachelor of sciences	Master degree
Severe deficiency of vitamin D	6%	55%	12.4%	23.4%	2.8%
Moderate deficiency of Vit D	9.1%	51.5%	21.1%	27.2%	0%
Mild deficiency of Vit D	0%	46.2%	7.7%	23.1%	23.1%
Normal vitamin D	0%	20%	0%	60%	20%

Table2-Frequency distribution of vitamin D deficiency in the mothers in terms of parity

	1st pregnancy	2nd pregnancy	3rd pregnancy
Severe deficiency of vitamin D	69.8%	23.9%	6.3%
Moderate deficiency of Vit D	63.6%	21.2%	15.2%
Mild deficiency of Vit D		80%	20%
Normal vitamin D		80%	20%

In this regard, there is a significant relationship between vitamin D deficiency and parity (P-value= 0.05), that is, the more parity, the less will be vitamin D deficiency. Likewise, there was a significant relationship between age and vitamin D deficiency (P-value= 0.05). This relationship is given in table3.

Table3-Relationship between age and vitamin D deficiency

	The mean of age rang	n	Housewife	Employed
Severe deficiency of vitamin D	25.4	217	76.6%	23.4%
Moderate deficiency of Vit D	26.1	33	71%	29%
Mild deficiency of Vit D	27.7	14	50%	50%
Normal vitamin D	33.4	5	20%	80%

In this regard, according to the distribution of maternal age and vitamin D deficiency, with increasing maternal age, vitamin D deficiency has decreased. Since P-value is 0.012, the relationship is significant so that vitamin D deficiency is less in employed mothers than the housewives. There was also a significant relationship between vitamin D level and maternal pre-pregnancy weight (P-value= 0.04), So that among the 280 mothers of our study, the mean age of the four groups mothers in their first trimester has been shown in table4.

Table4-the relation between pre-pregnancy weight and Vit D deficiency

	Pre-pregnancy weight	Weight in the first trimester

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Severe deficiency of vitamin D	60.67 Kg	60.98 Kg
Moderate deficiency of Vit D	63.5 Kg	63.15 Kg
Mild deficiency of Vit D	64.57 Kg	64.92 Kg
Normal vitamin D	65.4 Kg	66.2 Kg

This suggests that by increasing pre-pregnancy weight, vitamin D deficiency reduces. It shows that vitamin D level is more in the mothers who have gained more weight in their first trimester.

Therefore, the minimum and maximum values of weight in the first trimester of pregnancy have been 45 and 85 kg for the severe deficiency group, 50 and 79 kg for the moderate deficiency group, 53 and 75 kg for the mild deficiency group, and 60 and 73 kg for the normal group.

The study of 280 pregnant women in four groups of vitamin D and haemoglobin measurements showed that: in women with pregnancy anemia (Hb<11), the mean of vitamin D is 8.48 and in women with Hb>11, this mean is 19.32. In fact, of 280 pregnant women, 129 women's haemoglobin was lower than 11 and 141 women's haemoglobin was higher than 11.(table 5)

Table5-The relationship between the frequency of vitamin D deficiency and hemoglobin levels in the pregnant women

Vit D	Maximum hemoglobin	Minimum hemoglobin
0-20	14.30	7.80
20-40	13.40	10.30
40-60	15.60	11.50
Higher than 60	15.30	11.50

The frequency of toothache in 280 mothers of four groups of vitamin D is as follows: by increasing vitamin D, the incidence of toothache decreases, and P= 0.01 is significant, the results has been shown in table6.

Table6-The relationship between the frequency of vitamin D deficiency and the incidence of toothache in the pregnant women

Vit D	Pregnant women with toothache	Pregnant women without toothache
0-20	59.6%	40.4%
20-40	12.5%	87.5%
40-60	0%	100%
Higher than 60	0%	100%

Also the relationship between the frequency of vitamin D deficiency and the incidence of bacterial vaginosis has been shown in table 7.

Table 7-The relationship between the frequency of vitamin D deficiency and the incidence of bacterial vaginosis

Vit D	The incidence of BV	The absence of VB
0-20	82.2%	17.8%
20-40	53.1%	46.9%
40-60	30.8%	69.2%
Higher than 60	40%	60%

Discussion and Conclusion:

This study was conducted to examine vitamin D level in the first trimester of pregnant mothers and determine the relationship ofvitamin D deficiency with anemia, toothache and bacterial vaginosis. The initial number of subjects was 330 that because of confounding factors, 50 subjects were excluded from the study and the number of subjects was reduced to 280. In the study, no specific age was defined and all pregnant women with different ranges of age were randomly selected and included in the study. Of the study's subjects, the severe deficiency group has the highest frequency (80.3), indicating that a wide range of pregnant women suffer severe vitamin D deficiency (0-20).

In a study of Asian immigrant women living in London, like our study, the high prevalence of vitamin D deficiency has been reported. According to this study, 37 percent of pregnant

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women had less than 4 nmol/L vitamin D(Velagapudi, 2011). Likewise, in a study conducted by Eini et al. it was shown that vitamin D concentration in the first trimester of pregnancy has been less than 10 in 20% of women and less than 20 in 40% of women. Generally, in this study, it was declared that the overall deficiency of vitamin D has been 20% during pregnancy (Eini E, 2003). Hashemi-poor et al., in their study declared this deficiency between 9.6 and 57.6 percent (Hashemipor, 2004).

Educational level of mothers was categorized as under diploma, diploma, associate degree, bachelor degree and master degree. According to the results of this study, under diploma education was only observed in the mothers with severe and moderate vitamin D efficiency. That is, in the mothers with severe deficiency of vitamin D, 6% were under diploma and in the mothers with moderate deficiency, 9.1% were under diploma and those with mild deficiency and normal vitamin D level, had higher than diploma education. Although vitamin D level is higher in the women with a higher education, as P-value is 0.6, it is not significant that is perhaps due to the random selection of the subjects.

In Khouri et al.(1999) study on vitamin D, it was shown that there is a significant relationship between maternal age, maternal education, first pregnancy age, previous parities, the incidence of risk factors during pregnancy and vitamin D deficiency.

In four groups of study among the women with first pregnancy, no one was found with normal level of vitamin D. Most women in three groups of severe, moderate and mild Vit D deficiency have been experiencing their first pregnancy. This meanswhen the number of pregnancies increases, the percentage of vitamin D deficiency decreases, which may be because of better education, gaining more nutritional-related experiences and treatment with vitamin D supplements after the first pregnancy. Moreover, the current study showed by increasing maternal age, vitamin D deficiency reduces significantly during pregnancy (P= 0.05). In this regard, the mean age was 25.4 in the mothers of severe deficiency group, and 33.4 in the mothers of normal group.

In a study with a P-value of 0.012, there is a significant relationship between vitamin D level and pregnant mother's job,with a Chi-square of 6.342, the average vitamin D level is 12.25 in the housewife mothers and 14.01 in the working mothers, indicating that the level of vitamin D deficiency is less in the working mothers.

In the current study with the P-value of 0.04, there is a significant relationship between vitamin D deficiency and pre-pregnancy weight, so that pre-pregnancy average weight of the mothers with severe deficiency is 60.67 kg while this weight is 65.4 kg in the mothers of normal group. This suggests that vitamin D deficiency is less in the mothers with a higher pre-pregnancy weight. This study also showed that in the mothers who gained more weight during the first trimester of their pregnancy, vitamin D deficiency is less observed. In other words, the average weight of the mothers in the severe deficiency group is 60.98 kg, while it is 66.2 kg in the normal group.

In this study, the relationship between vitamin D level and the incidence of bacterial vaginosis was examined and it was found out that the incidence of bacterial vaginosis is less in the mothers with higher level of vitamin D.

Lip et al.(2006), in their study on monocyte cells in two groups with adequate and inadequate vitamin D, showed that the group with adequate vitamin D has greater anti-microbial activities.

Also in another study declared that the incidence of vitamin D-dependent catholicising protein can cause elimination of intracellular infections (Mehta S,2009). Bodnar et al.(2011) declared that vitamin D deficiency will lead to bacterial vaginosis in the first trimester of pregnancy.

In our study, the relationship between vitamin D deficiency and maternal haemoglobin level during the first trimester of pregnancy was evaluated. The results showed that by increasing vitamin D level, haemoglobin level also increases so that the mothers with normal vitamin D level has a higher haemoglobin level and the incidence of anemia is less in these women.

In a study conducted by William B et al. on the incidence of anemia, it was observed that the incidence of anemia has been about 12 percent in the pregnant women who suffered vitamin D

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deficiency in their first trimester of pregnancy(William B,2007).In another study with the P-value of 0.01, there has been a significant relationship between vitamin D deficiency and toothache in the first trimester, so that, in the women with vitamin D level of above 40, the incidence of toothache has been zero. On the other hand, the incidence of toothache has been 59.6% in the mothers who suffered severe vitamin D deficiency.

Vitamin D deficiency during pregnancy leads to 12% anemia in the first trimester and up to 50% anemia in the third trimester of pregnancy. Vitamin D deficiency can increase the risk of gestational diabetes up to 9%, the incidence of bacterial vaginosis up to 3.5%, influenza up to 2%, preeclampsia up to 5.2%, the incidence of sepsis 1.13% and toothache up to 2% (William B,2007).Likewise, Birth et al. estimated that the incidence of toothache in women with vitamin D deficiency is 21 percent (With,2008).

Conclusion and Recommendations:

Nutritional modification programs, especially for pregnant women, seem necessary. Eating the foods rich in micronutrients, particularly vitamin D, is recommended. Nutrients such as dairies, dietary enrichment and using vitamin D supplements are recommended for pregnant women. Given vitamin D deficiency during pregnancy and the maternal and fatal side effects that were referred in this study, it is recommended that vitamin D level be measured both before and during the first trimester of pregnancy. Given that most mothers suffered severe vitamin D deficiency, routine measurement of vitamin D is recommended during the first trimester of pregnancy, and scientific and therapeutic protocols must be adopted during the first trimester to compensate this deficiency.

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