Section: Obstetrics and Gynecology

Original Research Article

EFFECTS OF MATERNAL VITAMIN D DEFICIENCY ON PREGNANCY OUTCOMES-A COHORT STUDY

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Abstract

Background: Vitamin D deficiency is a common problem in women of reproductive age group and pregnant women. Aim of the study is to assess the relationship between vitamin D deficiency and adverse pregnancy outcomes. **Materials and Methods:** This was a prospective cohort study conducted in the department of Obstetrics and Gynecology of a tertiary care center in Kerala for a period of 1year. 60 pregnant women 30 with vitamin D deficiency(<20ng/ml) and 30 with vitamin D insufficiency (20 to 30 ng/ml) with gestational age 8-12 weeks were included in the study and followed up separately till child birth for the occurrence of any adverse pregnancy outcomes. **Result:** There was a statistically significant difference in mean age (years) of pregnant woman (vitamin D insufficient =29.37±4.279, vitamin D deficient = 26.53±4.790) p-0.012 and mean vitamin D levels in ng /ml (vitamin D insufficient= 21.317± 2.2685, vitamin D deficient = 12.000± 2.5034) p-(<0.01) between the two groups. 93.3% of the women in the deficient group and 76.6% of women in insufficient group developed adverse outcomes (p-0.010). This study was not powered to detect associations between vitamin D deficiency and individual adverse pregnancy outcomes. **Conclusion:** The adverse pregnancy outcomes were more in the vitamin D deficient pregnant women compared to vitamin D insufficient pregnant women. Younger women were at higher risk of developing vitamin D deficiency during pregnancy. Vitamin D supplementation in early pregnancy may help to avoid adverse pregnancy outcomes.

INTRODUCTION

Vitamin D deficiency has emerged as a common problem among women of reproductive age group as its prevalence is increasing in developing countries like India. Endocrine society has defined vitamin D deficiency as serum levels of 25-hydroxy vitamin D below 20 ng/ml.1 Vitamin D levels between 20 to 30 ng/ml is considered as insufficient. As per the studies conducted in various parts of India, the prevalence of vitamin D deficiency among healthy pregnant women was found to be high and it varied from 93-97%.[1] There are multiple factors that can lead to vitamin D deficiency during pregnancy, such as lack of adequate exposure to sunlight and low oral intake of vitamin D that are insufficient to meet the increased demands of pregnancy.[2] Due to the modifications of vitamin D metabolism during pregnancy, there is a 2-3 fold increase in the concentration of calcitriol (1,25-dihydroxy vitamin D3) during the initial weeks of pregnancy and it crosses the placenta and forms the major pool of vitamin D in the foetus.[3,4] The pharmacological actions of vitamin D in pregnancy include its effect on placental function and immune response. The serum levels of pro-inflammatory cytokines like tumor necrosis factor α (TNF-α), interleukin -6(IL-6) and interferon-γ(INF-γ) are found to be elevated in pregnant women with vitamin D deficiency.[5] As vitamin D is essential for maternal and fetal health during pregnancy; its deficiency can lead to adverse pregnancy outcomes. Adverse pregnancy outcomes that are related to vitamin D deficiency are, gestational diabetes mellitus (GDM), pregnancy induced hypertension, urinary tract infections, premature rupture of membranes, preterm delivery

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and Cesarean section.[3,4] Expression of 1-α hydroxylase enzyme and vitamin D receptor in the pancreatic ß cells suggest role of vitamin D in maintaining glucose tolerance. Hence vitamin D deficiency among pregnant women may be related to increased risk of GDM. The role of altered vitamin D metabolism in pregnant women with preeclampsia may be associated with the action of elevated inflammatory mediators in blood vessels. The mechanism of increased susceptibility to infection including urinary tract infection among pregnant women with vitamin D deficiency may be due to the impairment of vitamin D mediated signaling and induction of antimicrobial peptide cathelicidin from macrophages.[5] Vitamin D deficiency can induce preterm labor in pregnant women by affecting body inflammatory factor levels like prostaglandins that stimulate uterine contractions.[6] Higher risk of cesarean section was also observed among pregnant women with vitamin D deficiency which was hypothesized as due to reduced pelvic muscle strength causing prolonged labor. However, clinical studies establishing the association between vitamin D deficiency and adverse pregnancy outcomes have conflicting results due to paucity of clinical trials conducted in this area and heterogeneity of population studied.[5-8] Although there was evidence of vitamin D deficiency in women of reproductive age group in previous studies its effect on adverse pregnancy outcomes was not much studied. The objective of this study was to assess the relationship between vitamin D deficiency in early pregnancy and subsequent adverse clinical outcomes.

MATERIALS AND METHODS

This was a prospective observational study conducted in pregnant women aged 18 years or older, at 8 to12 weeks' gestation coming for antenatal checkup in the department Obstetrics and Gynecology, for a period of 1year. Approval from the Institutional Ethics Committee was taken to conduct the study. A written informed consent was obtained from all the participants included in the study. Women with history of chronic medical conditions like preexisting diabetes mellitus (type 1 or 2), neurological disorders, renal and cardiovascular diseases were excluded from the study. A pre prepared performa was used to collect data regarding patient demographics, vitals including body mass index (BMI), clinical examination findings, blood investigations and ultrasound sonography test (USG) reports at the initial visit. Gestational age of pregnant women was confirmed with ultrasound and verified by the gynecologist. Along with routine hematological examination serum vitamin D levels were measured at 8-12 weeks of gestation. Based on serum Vitamin D levels assessed during the first visit, pregnant women were considered either as Vitamin D insufficient group (vitamin D between 20 to 30 ng/ml) or as vitamin D deficient group (vitamin D <20nanogram/ml) till the sample size (30 in each group) was attained. Each cohort was followed up separately for the rest of gestational period till child birth for the occurrence of any adverse pregnancy outcomes like preeclampsia, gestational diabetes, preterm delivery, intra uterine growth retardation and spontaneous abortion. Preeclampsia and gestational diabetes were diagnosed as described in the American College of Obstetricians and Gynecologists practice bulletins. Preterm delivery was considered as a spontaneous preterm birth less than 37 weeks gestational age due to preterm labor or premature rupture of membranes and growth restriction was defined by estimated fetal weight less than the 10th percentile for gestational age. Spontaneous abortion was defined as spontaneous abortion in the first trimester after enrollment in the study. Statistical analysis was done using appropriate statistical package. Chi square analysis was performed on the categorical variables and analysis of variance (ANOVA) was performed on the continuous variables. P-value < 0.05 was considered as statistically significant.

RESULTS

A total of 60 pregnant women, at 8 to 12 weeks gestation visiting Obstetrics and Gynecology department, for antenatal check-up and diagnosed with vitamin D deficiency were included in the study. The mean age of pregnant women included in the study were 27.94±4.724 years.46.6 % of them were graduates and 60 % of them were working women. Majority of them (86.6%) followed a non-vegetarian diet. Pregnant women with vitamin D level between 20-30ng/ml was considered as vitamin D insufficient group and with vitamin D levels <20nanogram/ml were considered as vitamin D deficient group, 30 in each group. Demographics of the study participants in each group is shown in [Table 1].

There was a statistically significant difference in the mean age of pregnant women between the two groups (p-0.012). Distribution of maternal age in both groups is depicted in figure 1 and majority of pregnant women included in the study belonged to age group 25-29 years. In vitamin D deficient group 30% of pregnant women belonged to age group <25years and 46% of the belonged to age group 25-29 years. Hence according to the present study, younger women were at high risk of Vitamin D deficiency.

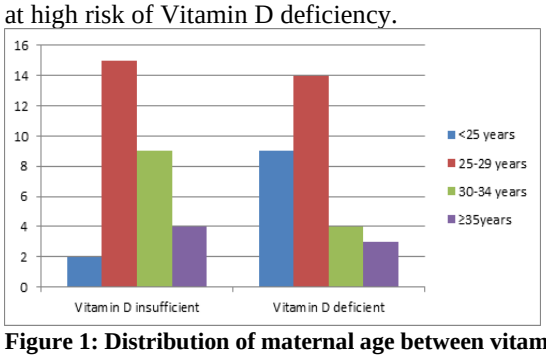

Figure 1: Distribution of maternal age between vitamin D Insufficient and Deficient groups

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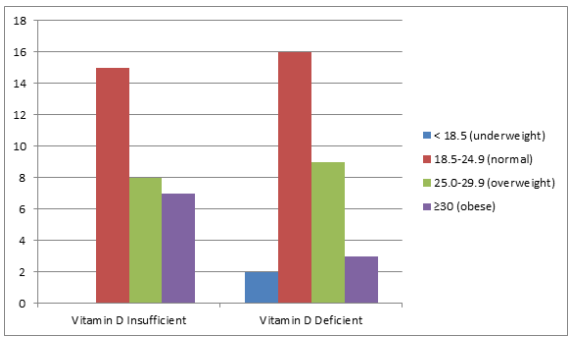

Figure 2: Comparison of vitamin D levels between Body mass index (kg/m2)

51.7% of the pregnant women included in study were primi-gravidae while 48.3 % of them were multi-gravidae. 85% of pregnant women included gave a history of regular menstrual cycles and 68.3% of them did not have any major illness in the past.

Comparison of clinical data between the Vitamin D insufficient and deficient groups is depicted in [Table 2]

The two groups were comparable with respect to clinical data except for plasma levels of vitamin D. There was a statistically significant difference between mean vitamin D values between the groups. Comparison of vitamin D levels between Body mass index groups (kg/m2) is shown in [Figure 2]

78.3% of the patients included in the study developed adverse pregnancy outcomes. 76.6% of the participants in the insufficient group developed adverse pregnancy outcomes while 93.3% of participants developed adverse outcomes in the deficient group. The difference in the distribution of composite adverse pregnancy outcomes between the two groups was found to be statistically significant (p-0.010). Distribution of adverse pregnancy outcomes between the groups is shown in [Table 3]

Table 1: Demographic pattern of pregnant women

	Total (N=60)	Vitamin D Insufficient group (n=30)	Vitamin D Deficient group (n=30)	p value*
Age (years) Mean±SD	27.94±4.724	29.37±4.279	26.53±4.790	0.012
	Total N (% of 60)	Insufficient group n (% of 30)	Deficient group n (% of 30)	p value
Graduates	28(46.6)	13(43.3)	15(50)	0.796
Working women	36(60)	20(66.6)	16(53.3)	0.430
Non vegetarians	52(86.6)	22(73.3)	30(100)	0.647

Table 2: Comparison of clinical data between the Vitamin D insufficient and deficient groups

Clinical characteristics	Total N (% of 60)	Vitamin D Insufficient group n (% of 30)	Vitamin D Deficient group n (% of 30)	p value
Primi gravida	31(51.7)	14(46.6)	17(56.6)	0.606
History of regular menstrual cycles	51(85)	28(93.3)	23(76.6)	0.145
No history of significant illness in the past	41(68.3)	24(80)	17(56.6)	0.095
	N=60 Mean±SD	n=30 Mean±SD	n=30 Mean±SD	p value
Gestational age at analysis (weeks)	38.68±.7569	38.60±.8060	38.777±.7070	0.411
BMI	24.91±5.078	25.948±5.797	23.877±4.0799	0.258
Vitamin D level (ng/ml)	16.658±5.2610	21.317± 2.2685	12.000± 2.5034	.000

Table 3: Comparison of adverse pregnancy outcomes between the Vitamin D insufficient and deficient groups

Adverse pregnancy outcomes	Total (N=60)	Vitamin D Insufficient group (n=30)	Vitamin D Deficient group (n=30)	p value
Nausea /vomiting	25(41.6)	10(33.3)	15(50)	.295
Spotting	2(3.3)	0(0)	2(6.6)	.492
Urinary tract infection	12(20)	4(13.3)	8(26.6)	.706
Pregnancy induced hypertension	8(13.3)	3(10)	5(16.6)	1.000
Gestational diabetes	20(33.3)	10(33.3)	10(33.3)	-
Intrauterine growth retardation	2(3.3)	0(0)	2(6.6)	492
Preterm labour	1(1.6)	0(0)	1(3.3)	1.000
Caesarean Section	25(41.6)	15(50)	10(33.3)	.295
PPH	4(6.6)	2(6.6)	2(6.6)	-

DISCUSSION

In the present study mean maternal age in vitamin D insufficient group and vitamin D deficient group was found to be29.37± 4.279 years and 26.53± 4.790 years respectively. In this study younger women were at high risk of Vitamin D deficiency which goes in agreement with the study done by Al Faris NA et al,[9] which found that younger women had a significantly higher risk of hypo-vitaminosis D than older women. This finding might be due to more vitamin D supplement taken by older women compared to younger women. Vitamin D deficiency in younger women could be related to frequent consumption of energy-dense foods such as fast foods and soft drinks which are poor sources of vitamin D5 and low consumption of healthy foods that contain reasonable amounts of vitamin D.[10] In the present study there was no significant difference in the number of graduates and working women across the two group hence the working status of pregnant was not considered as a risk factor for development of vitamin D deficiency. Study done by Sowah, D et al also suggested that prevalence of vitamin D

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deficiency among working population was not entirely explained by sunlight exposure.[11] In a study done by Shrestha D et al,[12] 85.71% of pregnant woman with vitamin D deficiency were non-vegetarians which goes in agreement with present study. In this study the percentage of primi-gravida was higher in vitamin D deficient group (56%) compared to that in vitamin D insufficient group (46%). This finding was supported by the study done by Ahmed F et al,[13] in which mean serum vitamin D level was significantly lower among nulliparous pregnant women than multiparous pregnant women and this could be due to the vitamin D supplements taken during previous pregnancies. In their study, Shrestha D et al also found that majority of pregnant woman with vitamin D deficiency were primigravidae.[12] The two groups were also comparable with respect to order of pregnancy, menstrual history and other significant illness in the past which can affect the vitamin D levels. There was no significant difference in gestational age of participants between the two groups. In the present study mean BMI was found to be less in vitamin D deficient group and compared to that in vitamin D sufficient group. 51.6% of the pregnant women had normal BMI while 28.3% of them were overweight and 16.6% of them were obese. 70% of the obese pregnant women belonged to vitamin D insufficient group. On the contrary in a study done by Vranic L et al it was found that there was a negative relationship between plasma vitamin D levels and BMI and they proposed that dilution of vitamin D in a large volume of fat is the reason for the negative relationship. Although the amount of vitamin D is similar in obese and lean subjects, the plasma concentration will be less in obese because of larger volume of distribution. However the relation between obesity and serum vitamin D levels may vary by race/ethnicity.[14]

The mean vitamin D level in this study was found to be 12.000± 2.5034 ng/ml in the vitamin D deficient group and 21.317± 2.2685 ng/ml in vitamin D sufficient group. The findings of a similar study done in North Eastern India,[5] correlates well with that of present study in which mean Vitamin D level in the Vitamin D deficient group was 12.91 ng/dL and 24.175 ng/dL in the insufficiency group. 93% of the patients in the deficient group developed adverse pregnancy outcomes while 76% of patients developed adverse outcomes in the insufficient group and the difference was found to be statistically significant as reported by Menon M et al in their study which showed lesser number of adverse pregnancy outcomes in the vitamin D insufficient group compared to deficient group.[3] Study done by Pirdehghan A et al also got similar results which proved that vitamin D deficiency was prevalent in pregnant women and it was significantly associated with adverse pregnancy outcomes.[15]

CONCLUSION

The adverse pregnancy outcomes were more in the vitamin D deficient pregnant women compared to vitamin D insufficient pregnant women and younger women were found to be at higher risk of developing vitamin D deficiency during pregnancy. This study was not powered to detect associations between vitamin D status and these individual complications of pregnancy. However, the high percentage of affected individuals highlights the impact of vitamin D deficiency in young, healthy reproductive-aged women.

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