Original Research Article

A prospective observational study of effect of vitamin d deficiency on adverse pregnancy outcome in a tertiary care hospital

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Received: 22-05-2021 / Revised: 25-06-2021 / Accepted: 24-07-2021

Abstract

Introduction: Vitamin D is a part of complex steroid hormone system long known to be involved in the bone metabolism. Recently, the prevalence of rickets has increased sparking a new interest in vitamin D deficiency. In addition, studies of Vitamin D physiology suggest that effects of Vitamin D deficiency could be much broader than rickets including cardiovascular diseases, cancers, Diabetes, Infection, allergy and other pregnancy complications. **Materials and Methods:** A hospital based cross-sectional, observational study was carried out in the Department of OBG in Government General Hospital, Ananthapuramu. 100 pregnant women admitted in third trimester in labor ward were enrolled in the study. Study period was from January 2020 to December 2020. All pregnant women were subjected to testing serum Vitamin D at term after counselling and informed consent. **Results:** The present study was done on 100 patients admitted in labor ward in the Department of OBG in Government General Hospital, Ananthapuramu. Table1 shows the sociodemographic profile of patients according to the level of Vitamin D. Majority of the patients were>30 years (31.82%), completed Secondary school education (54.55%), House wife (86.36%), middle income group (65.91%), less exposure to sun (63.64%), not supplemented with Vitamin D (90.90%), multigravida (68.18%) and urban (72.73%) in Vitamin D Deficient group (Table1). Table 2 shows only (12%) pregnant women were Vitamin D sufficient and Vitamin D deficient and insufficient group were (88%). **Conclusion:** Our study shows high prevalence of Vitamin D deficiency in pregnant women and complications with pregnancy were less prominently seen in Vitamin D deficient group like PROM, preterm labor, Diabetes, Gestational Hypertension, increased Caesarian section rate and thus fails to show a direct relation between low maternal vitamin D level and adverse fetal outcome.

Key Words: Vitamin D, physiology, PROM, preterm labor, Diabetes, Gestational Hypertension.

Introduction

Vitamin D is a part of complex steroid hormone system long known to be involved in the bone metabolism. Recently, the prevalence of rickets has increased sparking a new interest in vitamin D deficiency. In addition, studies of Vitamin D physiology suggest that effects of Vitamin D deficiency could be much broader than rickets including cardiovascular disease, cancers, Diabetes, Infection, allergy and other pregnancy complications[1].During pregnancy, serum level of 1, 25 (OH) D increase up to twofold starting at 10-12 weeks of gestation and reaches to a maximum level in the third trimester.

Given an increase in the active form of Vitamin D, pregnant women are likely to have a higher cellular exposure to Vitamin D during second and third trimesters suggesting a role for Vitamin D for well-being in obstetrics. Perinatal outcome to be related to Vitamin D deficiency preeclampsia, Gestational Diabetes mellitus, low birth weight, preterm delivery, and increased caesarian section rate. There is a wide range of actions of vitamin deficiency in pregnancy, including its effects on placental function and inflammatory response [2].

Proinflammatory cytokines, such as Tumor necrosis factor-a, Interleukin-6, and Interferon-gama have been reported to be increased in pregnancies with Vitamin D deficiency. Having important immune-modulated property, vitamin D may help to setup a proper maternal immune response to placenta.

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It also regulates key target genes associated with proper implantation of placenta. Vitamin D regulates expression of Human chorionic gonadotropin in syncytiotrophoblast and stimulates production of sex steroids. Many studies also suggest that vitamin D has important role in glucose and insulin metabolism[3].Pancreatic β-cells express 1-α-hydroxylase; The active form of vitamin D binds on vitamin D receptor on pancreatic β-cells; The vitamin D response element is present in the human insulin gene promoter. There is also number of evidences about the role of vitamin D in maintaining glucose tolerance through its influence on insulin secretion and sensitivity[4].

The exact mechanism of altered vitamin D metabolism in patients with preeclampsia and hypertensive disorders is not fully understood. It may be related with inflammatory mediators and effects on blood vessels[5]Vitamin D could influence the pathophysiology of preterm labor as it affects the processes of inflammation and immuno-modulation. The susceptibility to infection is increased in cases of vitamin D deficiency because of impairment of toll-like mediated induction of antimicrobial peptide cathelicidin from macrophages[6].A possible reason for the potential higher risk of caesarian delivery in women with lower vitamin D concentrations was hypothesized to be reduced pelvic muscle strength leading to prolonged labor.India being a tropical country with ample sunlight throughout the year, people still suffer from vitamin D deficiency which is worsening in pregnancy.

Materials and methods

Study Design

Hospital based cross-sectional, observational study.

Study location

Department of OBG in Government General Hospital, Ananthapuramu.

Study Duration

January 2020 to December 2020.

A hospital based cross-sectional, observational study was carried out in the Department of OBG in Government General Hospital, Ananthapuramu. 100 pregnant women admitted in third trimester in labor ward were enrolled in the study. Study period was from January 2020 to December 2020. All pregnant women were subjected to testing serum Vitamin D at term after counselling and informed consent.

Inclusion Criteria

All pregnant women at term irrespective of age and parity

Exclusion criteria

Pregnant women with active Thyroid diseases like Thyroiditis or Grave's disease, preexisting Calcium or Parathyroid condition or who require diuretic or cardiac medication therapy including Calcium channel blockers.

100 patients were included in the study from 28 weeks to 40 weeks of gestational period. Information on age, education, parity, occupation, income and obstetric history was obtained from the mother using a questionnaire. Gestational age (in weeks) was calculated from the first day of the last menstrual period. History of iron and calcium intake was also taken. Blood investigations like Hemoglobin, and serum vitamin D were done. High risk factors like anemia, preeclampsia, Diabetes, were identified. Patients were followed-up for delivery events like Normal Vaginal delivery, increased Caesarian section rate and birth outcomes like birth weight, APGAR Score and neonatal admissions to NICU were recorded. Analysis of plasma vitamin D was done. The deficiency value of vitamin D was less than 20ng/ml, Insufficiency (20-30ng/ml), Sufficiency (30-100ng/ml).

Data was analyzed by SPSS-18 Version. Data was expressed as frequency and percentage (%), Association between Vitamin D Category, demographic variable, Mode of Delivery, Maternal outcome and Neonatal outcome was assessed by Chi Square type/fisher exact type.* (S)=Significant* (NS)=Not Significant A P-Value of 0.05 or less was considered statistically significant.

Results

The present study was done on 100 patients admitted in labor ward in the Department of OBG in Government General Hospital, Ananthapuramu.

Table1. shows the sociodemographic profile of patients according to Vitamin D. Majority of the patients were>30 years (31.82%), completed Secondary school education (54.55%), House wife (86.36%),middle income group (65.91%), less exposure to sun (63.64%), not supplemented with Vitamin D (90.90%), multigravida (68.18%) and urban (72.73%) in Vitamin D Deficient group (Table1). Table 2 shows only (12%) pregnant women were Vitamin D sufficient and Vitamin D deficient and insufficient group were (88%). Total Vaginal deliveries (42%), (34%) in Vitamin D deficient patients and 8% in Vitamin D sufficient patients. Total Caesarian sections (58%), (54%) in Vitamin D deficient and (4%) in Vitamin D sufficient group Table-3. Table 4 summarizes the Pregnancy without complications seen in Vitamin D deficient group (55.0%) and (33%) with complications. Pregnancy with complications in deficient group include Preterm labour (39.39%), PROM (18.18%), infection (15.15%), GDM (12.12%), Preeclampsia (6.06%) and preexisting hypertension (9.09%). Table 5 shows Live birth (94.31%) in Vitamin D deficient group and (91.67%) in sufficient group. IUD in sufficient group (8.33%) and in Vitamin D deficient group (5.68%). Live birth in Vitamin D deficient group in term of weight of baby <2.5% Kg (13.25%) and >2.5 kg (86.75%). APGAR score <7 in deficient group (18.07%) and APGAR score >7 (81.92%). NICU admissions in Vitamin D deficient group (21.69%) and in Vitamin D sufficient (18.18%).

Table 1: Patient Demographics

Variables	Total (n= 100)	Vitamin D deficient (n = 88)	Vitamin D Sufficient (n= 12)	P-Value
Age <30yr	69%	60(68.18%)	9(75.0%)	0.750(NS)
Age >30yrs	31%	28(31.82%)	3(25.0%)	
Education				
Primary-sec	46%	40(45.45%)	6(50.0%)	0.769(NS)
>Secondary	54%	48(54.55%)	6(50.0%)	
House wife	86%	76(86.36%)	10(83.34%)	0.674(NS)
Working	14%	12(13.64%)	2(16.66%)	
Income				
Low	18%	10(11.36%)	8(66.66%)	0.000(S)
Middle	60%	58(65.91%)	2(16.66%)	
High	22%	20(22.73%)	2(16.66%)	
Exposure to sun				
More	42%	32(36.36%)	10(83.34%)	0.003(S)
Less	58%	56(63.64%)	2(16.66%)	
Supplement				
Yes	18%	8(9.09%)	10(83.34%)	0.000(S)
No	82%	80(90.90%)	2(16.66%)	
Number of gravida				
Primiparous	36%	28(31.82%)	8(66.66%)	0.026(S)
Multiparous	64%	60(68.18%)	4(33.34%)	
Rural	33%	24(27.27%)	9(75.0%)	0.002(S)
Urban	67%	64(72.73%)	3(25.0%)	

Table 2: Vitamin D Status

S.No	Vitamin D status	Number	Percentage
1	<30ng/ml	88	88%
2	>30ng/ml	12	12%

Table 3: Mode of Delivery

S.No	Total deliveries N=100	Vitamin D deficient (N=88)	Vitamin D Sufficient (N=12)	P-value
1	Vaginal Delivery N=42	34 (34%)	8 (8%)	0.213 (NS)
2	Caesarian Section N=58	54 (54%)	4 (4%)	0.116 (NS)

Table 4: Maternal Outcome

Vitamin D status	Pregnancy without complications (n = 64)	Pregnancy with complications (n = 36)	P value
Vitamin D Sufficient (n = 12)	9 (9%)	3 (3%)	0.529 (NS)
Vitamin D deficient (n = 88)	55 (55%)	33 (33%)	-

Pregnancy with complications (n=36)						
Vitamin D Status	**Preterm labour**	**PROM**	**Infection**	**Gestational Diabetes**	**Pre eclampsia**	**Pre existing hypertension**
Vitamin D sufficient (n=3)	Nil	Nil	2 (66.66%)	Nil	Nil	1 (33.33%)

Table 5: Neonatal outcome

Vitamin D status	Live birth	IUD	P-Value
Vitamin D sufficient (N=12)	11 (91.67%)	1 (8.33%)	0.529 (NS)
Vitamin D deficient (N=88)	83 (94.31%)	5 (5.68%)	
Live Births(n=94)			
	Vitamin D sufficient (n=11)	**Vitamin D deficient (n=83)**	**P-value**
Birth weight <2.5 kg (n=12) >2.5 kg (n=82)	 1(9.09%) 10(90.90%)	 11(13.25%) 72(86.75%)	1.000 (NS)
APGAR < 7 (n=16) >7 (n=78)	 1(9.09%) 10(90.90%)	 15(18.07%) 68(81.92%)	0.683 (NS)
NICU Admitted (n=20) Not admitted (n=74)	 2(18.18%) 9(81.82%)	 18(21.69%) 65(78.31%)	1.000 (NS)

Discussion

Demographic status

Mother dressing habit, low dietary Vitamin D intake, not taking Vitamin supplementation during pregnancy, spending most of the day time indoors at home contribute to Vitamin D deficiency.

Table 1. shows, Vitamin D deficiency was more common in age <30 years (68.18%, P=0.75), House wife (8%, P = 0.674), completed secondary school education group (54.55%, P= 0.76), Less exposure to sunlight (63.64%, P =0.003), No supplementation of Vitamin D (90.90%, P =0.000), Urban group (72.73%, P =0.002) and middle income group (65.91%, P =0.000) and Vitamin D deficiency in multiparous (68.18%, P =0.026). Our study shows statistically significant association with Vitamin D in less exposure to sun light, no supplementation with Vitamin D, middle income group and in multiparous patients.

Study conducted by Andiran et al, found Vitamin D deficiency in low socioeconomic group where as Atiq et al found lower level serum level of Vitamin D in mother and in their infants from upper socio-economic group, who mostly preferred to live in indoor and reduced exposure to direct sun light14. In our study we found no correlation between the number of pregnancies and Vitamin D deficiency. Although more Vitamin consumption is expected in frequent pregnancies. If exposure to sunlight is not optimal, the Vitamin D content of diet must be 400IU/day[7]. Table 2 shows Vitamin D deficiency was even more marked in our study, with third trimester level lower than<30 ng/ml in 88% of the patients. The finding was similar to the study conducted by I.Pehlivan, S.hatun et al in 200015. In August 1998, in a study performed in Istanbul, Alagol et al, reported low serum25-hydroxy vitamin in D3 in 66% of women of reproductive age 16. The study done by Dava A et al (2017) revealed that prevalence of Vitamin-D deficiency was 48.2% among pregnant women[8].Table 4 summerizes the maternal outcome seen in Vitamin D deficient group (55.0%, P=0.529) without complications and this association is not statistically correlated. Pregnancy with complications in deficient group include Preterm labour (39.39%), PROM (18.18%), Infection (15.15%), GDM (12.12%), Preeclampsia ((6.06%) and preexisting hypertension (9.09%).

Pre-eclampsia

In our study, reported number of Pre-eclampsia(6.06%) and Hypertensive disorder (9.09%) with pregnant patient were less but Serum level of Vitamin D level of all these patients was<20ng/dl. So further larger studies in this perspective would be needed. Parul Singla et al studied in 100 pregnant women who received 60,000 IU every fortnightly from 28week till 36 week of gestation. Vitamin D supplementation during third trimester of pregnancy was found to be efficacious in reducing the risk of Pre-eclampsia by increasing therapeutic effectiveness of Calcium supplementation in pregnant women[9].

Impaired glucose tolerance

The risk of glucose tolerance depends on the variations of ethnicity. In a majority of non-Hispanic white population, 25 (OH)D concentrations at 16 weeks of gestation were significantly lower in GDM subjects than in controls, whereas no association was found in Indian mothers where 25 (OH)D concentrations were measured at 30 weeks of gestation. In our study, reported number of Gestational diabetes were less (12.12%) and all had vitamin D deficiency. This is a very small sample size to comment on the association of glucose tolerance and vitamin D deficiency.

Neonatal out come

In our study maternal Vitamin D levels had no Statistical correlation with birth weight (P=1.000), APGAR Score (P=0.683) and NICU admissions (P=1.000). However, multiple confounding factors could be implicated for the Vitamin D effects on gestational baby size (such as ethnicity, nutritional status, sunlight exposure) milk or calcium intake. A randomized trial was conducted in France in 3 groups of pregnant women in the third trimester: 1st group received 200,000 IU of Vitamin D in a single dose, 2nd group received 1000 IU of Vitamin

D daily and 3rd group served as the control. No differences in birth weight were found among groups. In contrast, a pregnant women with Vitamin D intakes < 200IU/d had infants with birth weighs that were 60 g below than women with Vitamin D intakes at or above 200IU/ d.

Conclusion

This study, after summarizing existing data shows high prevalence of Vitamin D deficiency in pregnant women and complications of pregnancy like PROM, Preterm labor and increased rate of Caesarian section, Gestational hypertension, pre-eclampsia and Diabetes were not prominently seen with pregnancy in Vitamin D deficiency and fails to show a direct relation between low vitamin D level and adverse neonatal outcome in our study.

On the contrary many scholars and researchers have now started questioning the association of vitamin D deficiency with every medical disorder possible. For that matter associations have been reported regarding pregnancy related complications. It is now thought to raise the normal level criteria for vitamin D. Vitamin D deficiency and associated complications are seen very rarely in the individuals unless the deficiency is very severe. Hence to conclude, our study fails to show a relation of vitamin D deficiency with other high risk factors of pregnancy and adverse fetal outcome. But supplementation of Vitamin D is simple and cost effective with a low likelihood of toxicity. We recommend to increase supplementation of Vitamin-D or exposure to sun light in all pregnant women to keep serum level of25 (OH) D in the normal range for adult (>30ng/ml).

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Conflict of Interest: Nil
Source of support: Nil