ORIGINAL RESEARCH

Vitamin d level in preeclampsia and eclampsia and its correlation with fetomaternal outcome

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ABSTRACT

Background: Vitamin D deficiency during pregnancy is associated with the non-classical action of this hormone, being linked with preeclampsia, insulin resistance, gestational diabetes mellitus and increased risk for caesarean section delivery. Vitamin D deficiency has been hypothesized to be associated with low birth weight and admission to NICU. **Aim:** To study prevalence of vitamin D deficiency in pregnancy and its correlation with the maternal complications and evaluate perinatal outcome.**Material and Methods:** Total 100 patients were studied for vitamin D levels and associated obstetrical complications and risk factors over a period of one year. 88 pregnant women were found to be deficient with vitamin D.**Result:** 88 pregnant women out of 100 were deficient in Vitamin D levels. Maximum patients were less than 30 years of age, Vitamin D deficiency more in house wife (86.36%),multiparous (68.0%),Cesarean section (54%) in deficient group, Pregnancy with complication (33.0%) like preeclampsia, Gestational hypertension, PROM were less prominently seen in deficient group. Neonatal outcome like birth weight (86.75%)>2.5 Kg and <2.5kg (13.25%), NICU admission (21.69%) in Vitamin D deficient group.**Conclusion:** Our study show high prevalence of Vitamin D deficiency in pregnant women and complication with pregnancy were less prominently seen in Vitamin D deficient group like PROM, preterm labor, Diabetes, Gestational Hypertension, Cesarean section rate and thus fails to show a direct relation between low maternal vitamin D level and adverse fetal outcome.

Key words: Fetal and maternal outcome, pregnancy, Vitamin D

INTRODUCTION

Vitamin D deficiency is prevalent in India, a finding that is unexpected in a tropical country with abundant sunshine. Vitamin D deficiency is recognized as the most untreated nutritional deficiency currently in the world[1].

Several clinical studies suggest the possible association between low Vitamin D levels and potential adverse outcome of pregnancy[2,3]. In the last three years, an increasing amount of research suggests that some of the damage done by vitamin D deficiency is done in -utero while the fetus is developing. Much of that damage may be permanent, it cannot be fully reversed by taking Vitamin D after birth. The prevalence of Vitamin D deficiency has been reported to range from15%to 80%.[4]

The naturally occurring form of Vitamin D in human is cholecalciferol or Vitamin D3[5, 6].

Increased 25 (OH)D is first hydroxylated in the Liver. The second hydroxylation to the active from 1, 25 (OH)D occurs mostly in the Kidney in a process tightly regulated by calcium, Phosphorus and parathyroid hormone levels[7].

Vitamin D itself is devoid of any biological activity, but enzymatic conversion to [1,25 (OH) 2D] generates the hormonal form with diverse Biological activities. The action of 1,25 (OH)2D are mediated through specific, high affinity binding to the Vitamin D receptor (VDR), which is present in multiple tissue including placenta suggesting a farther- reaching role for VD than bone metabolism alone[8].

During pregnancy, serum level of 1, 25 (OH)D increased up to 2fold starting at 10-12 weeks of gestation and reaching a maximum in the third trimester[5]

Calcium is transported from the mother to the fetus through the placenta. Approximately 25-30g of calcium are transfer to the fetal Skelton by the end of the pregnancy most of which is transferred during the last trimester. Notably, the 24,25 (OH)2D synthesized by the placenta accumulates in bone may be involved in ossification of fetal Skelton[9].

Identifying Vitamin D deficiency by the circulating concentration of 25 (OH)D, the indicator of nutritional Vitamin D status. There is no consensus about the optimal 25 (OH)D level, but many experts accept a range 75 nmol/L (>30ng/ml) as optimal and serum Vitamin D level below 50 nmol/L (20ng/ml) represent deficiency.[10]

In its 2011 report, the Institute of Medicine (IOM) recommended 600 IU per day of 25 (OH)D for pregnant women specially to support bone metabolism and no more than 4000 IU per day to avoid hypercalcemia. American College of obstetricians and Gynecologist (ACOG) endorses these recommendations and propose 1000- 2000 IU per day of 25 (OH)D when deficiency is identified (<20ng/ml). Vitamin D deficiency during pregnancy is associated with the non-classical action of this hormone, being linked with pre-eclampsia, insulin resistance, gestational diabetes mellitus and increased risk for caesarean section delivery. Vitamin D deficiency has been hypothesized to be associated with low birth weight and admission to NICU.

AIM: To study prevalence of vitamin D deficiency in pregnancy and it correlation with the maternal complications and evaluate perinatal outcome.

MATERIAL AND METHODS

A hospital based cross-sectional, observational study was carried out in the Department of OBG in a tertiary care hospital, central India. 100 pregnant women admitted in third trimester in labor ward were enrolled in the study.

The study period was from last September 2021 to August 2022. All pregnant women were subjected to testing serum Vitamin D at term after counseling and informed consent.

INCLUSION CRITERIA: All pregnant women at term irrespective of age and parity.

EXCLUSION CRITERIA: Pregnant women with active Thyroid disease like Thyroid disease like thyroiditis or Grave's disease, preexisting Calcium or Parathyroid condition or who require diuretic or cardiac medication therapy including Calcium channel blocker.

DATA COLLECTION: 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 was done. High risk factors like anemia, preeclampsia, diabetes, were identified. Patients were followed-up for delivery events like Normal Vaginal delivery, Caesarean section and birth out comes like birth weight, APGAR score and neonatal admission to NICU were recorded.

Analyses of plasma vitamin D were done. The deficiency value of vitamin D was less than 20ng/ml, insufficiency (20- 30ng/ml), sufficiency (30-100ng/ml).[11, 12]

STATISTICAL ANALYSIS: 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. A P-Value of 0.05 or less was considered statistically significant.

RESULTS

The present study was done on 100 patients admitting in labor ward in department of Obstetrics and Gynecology, IGIMS, Patna.

Table1. Shows the sociodemographic profile of patients according to Vitamin D.

Majority of the patients were>30 years (31.82%), Secondary educated (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 (88%).

Total Vaginal delivery (42%), (34%) in Vitamin D deficient patients and 8% in Vitamin D sufficient patients. Total Cesarean section (58%), (54%) in Vitamin D deficient and (4%) in Vitamin D sufficient group Table-3. Table 4 summarizes the Pregnancy without complication seen in Vitamin D deficient group (55.0%) and (33%) without complication. Pregnancy with complication 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 show 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 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 admission in Vitamin D deficient group (21.69%) and in Vitamin D sufficient (18.18%).

Table1: Demographic factors of the study participants

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

*(S)=Significant, (NS)=Not Significant

Table2: Show Vitamin D Status

Vitamin D Status	Number	Percentage
<30ng/ml	88	88%
>30ng/ml	12	12%

Table3: Mode of Delivery

Total deliveries N=100	Vitamin D deficient (N=88)	Vitamin D Sufficient (N=12)	P-value
Vaginal Delivery N=42	34 (34%)	8 (8%)	0.213 (NS)
Cesarean Section N=58	54 (54%)	4 (4%)	0.116 (NS)

Table4: Maternal outcome

Vitamin D Status	Pregnancy without complication (n = 64)		Pregnancy with complication (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	**PretermLabour**	**PROM**	**Infection**	**Gestational Diabetes**	**Pre ecclampsia**	**Pre existing hypertension**
Vitamin D sufficient (n=3)	Nil	Nil	2 (66.66%)	Nil	Nil	1 (33.33%)
Vitamin D deficient (n=33)	13 (39.39%)	6 (18.18%)	5 (15.15%)	4 (12.12%)	2 (6.06%)	3 (9.09%)

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 Birth(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, no Vitamin supplementation during pregnancy spending most of the day time during 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), >secondary educated 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.* [13], 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 light[14]. 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.

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 2000[15]. In August 1998, in a study performed in Istanbul, Alagol*et al*., reported low serum25 -hydroxyvitamin in D3 in 66% of women of reproductive age[16]. The study done by Dava A *et al*. (2017) revealed that Vitamin D deficiency prevalence was 48.2% among pregnant women[17].

Table 3 shows the mode of deliveries in study subject. In our study cesarean section rate (54%, P = 0.2) were more than Normal Vaginal Delivery (34%, P = 0.213) in Vitamin D deficient group. Our study was similar to study conducted by Dave *et al*. (2017), shows an association of vitamin D deficiency and cesarean deliveries. 23.5% women delivering by cesarean had vitamin D deficiency but this association is not statistically correlated. Segregating the vitamin D deficiency with the indications of cesarean section will be more important to understand the role of vitamin D in initiation of labor or association with the calcium metabolism. Vitamin D deficiency (< 37.5 nmol/l) has been associated with a four-fold increased risk of primary caesarean section, although this has not been demonstrated in all studies. Merewood*et al*. measured vitamin D concentrations of 253 mothers after delivery[18]. They reported that the risk for primary cesarean section in women with vitamin D concentrations <37.5 nmol/L was almost four times higher than women with higher vitamin D concentrations. They proposed maternal vitamin D status may be associated with risk for primary cesarean section through calcium's role in the initiation of laboror by increasing preeclampsia risk. Studies revealed a significant increase in maternal serum calcium concentration.

Table 4 summerizes the maternal outcome seen in Vitamin D deficient group (55.0%, P=0.529) without complication and this association is not statistically correlated. Pregnancy with complication 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%).

PREECLAMPSIA: In our study, reported number of Pre-eclampsia (6.06%) and Hypertensive disorder (9.09%) with pregnancy patient were less but Serum level of Vitamin D level of all these patient was<20ng/dl. So further large studies in this perspective would be needed. Parul Singla *et al.* [19] studied in 100 pregnant women who received 60,000 IU every forth nightly from 60,000 IU every forth nightly 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.

IMPAIRED GLUCOSE TOLERANCE: The risk

of glucose tolerance depends on the variations of ethnicity. In a majority 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[20]. 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 OUTCOME: In our study maternal Vitamin D levels had no Statistical correlation with birth weight (P=1.000), APGAR Score (P=0.683) and NICU admission (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:1 group received200,000 IU of Vitamin D in a single dose, 1 group received 1000 IU of Vitamin D daily and 1 group served as the control. No differences in birth weight were found among groups[21]. In contrast, pregnant women with Vitamin D intakes< 200IU/d had infants with birth weighs that were 60 g below women with Vitamin D intakes at or above 200IU.

CONCLUSION

This study, after summarizing existing data show high prevalence of Vitamin D deficiency in pregnant women and complication of pregnancy like PROM, Preterm labor and rate of Caesarean section, Gestational hypertension, preeclampsia 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.

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 is simple and cost effective with a low likelihood of toxicity. We recommended increase supplementation or exposure to sun light in all pregnant women to keep serum level of25 (OH) D in the normal range for adult (>30ng/ml).

CONFLICTS OF INTEREST: None.

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