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Research Article

VITAMIN D DEFICIENCY IN PREGNANCY: EFFECT ON MATERNAL AND FETAL OUTCOME

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ABSTRACT

Objective: Vitamin D deficiency (VDD) during pregnancy is known to affect the neonatal morbidity and mortality. This study was conducted in pregnant women with the aim of assessing the prevalence of VDD in pregnant women and its effect on expecting mother and newborn.

Methods: This was a cross-sectional study done over a period of 2 years. 25(OH)D3 level was tested by Chemiluminescent Immunoassay in clinical biochemistry laboratory. Subjects were classified into Vitamin D-deficient, insufficient, and sufficient group.

Results: Mean level of Vitamin D in the study population was 21.82±12.95. The level of Vitamin D was found to be sufficient only in 28% (28/100) of subjects. A significant correlation was observed between newborn birth weight and serum Vitamin D level of the mother. Appearance, pulse, grimace, activity, and respiration (APGAR) score was moderately and severely depressed in 17% and 3% of babies, respectively. Pre-eclampsia was observed in 8% (8/100) of the subjects. A significant correlation was observed between the occurrence of pre-eclampsia and maternal Vitamin D. APGAR score was found to be significantly associated with serum Vitamin D.

Conclusion: There is a high prevalence of VDD in pregnant women. VDD in pregnancy is associated with several complications to the expectant mother as well as the fetus. Complications such as pre-eclampsia, low birth weight (LBW) babies, and low APGAR score were observed in the present study. There is a need of extensive clinical research on the impact of VDD in pregnancy on mother and fetal health.

Keywords: Vitamin D deficiency, Pregnancy, Maternal and fetal outcome, Pre-eclampsia, Appearance, pulse, grimace, activity, and respiration, Low birth weight.

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INTRODUCTION

Vitamin D is synthesized in skin and performs various physiologic functions in the body. Apart from its classical action of regulating calcium and bone metabolism, it has been found to be involved in immune-modulation, cell proliferation, cell differentiation, and in metabolic functions in diverse tissues and organs, including the brain, pancreas, and heart [1,2].

Vitamin D has a wide range of actions in pregnancy, including its effects on placental function and inflammatory response [3]. Vitamin D deficiency (VDD) remains a global under-diagnosed and under-treated nutritional deficiency among children, adults, and pregnant women along with their neonates [4-7]. Studies in India have reported a prevalence of VDD over 90% among antenatal population [8-11]. Various factors are known to affect Vitamin D concentration in body such as geographic location, climate, seasonal changes, diet, exposure to sunlight, skin pigmentation, socioeconomic and cultural constraints, and outdoor activity [12,13].

The requirement of Vitamin D during pregnancy and lactation is increased [10]. Vitamin D is transferred from pregnant mothers to their fetus and thus, it has the potential to influence development of the fetus. VDD during pregnancy has many health implications on both expectant mother as well as newly borne baby. Expectant mothers with VDD are at increased risk of pre-eclampsia, gestational diabetes mellitus, preterm labor, premature rupture of membranes (PROM), and preterm PROM, whereas newborns are likely to suffer from low birth weight (LBW), intrauterine growth restriction, neonatal tetany, neonatal jaundice, and congenital and infantile rickets [14,15].

VDD during pregnancy is known to affect the neonatal morbidity and mortality [12,16,17].

VDD especially during late pregnancy is associated with adverse fetal outcome as evidenced by low appearance, pulse, grimace, activity, and respiration (APGAR) score [18,19].

In the recent years, Vitamin D is one of the micronutrients which have gained massive interest in the fields of health and biomedical research community. There is a dearth of studies assessing the prevalence of VDD and its impact on maternal and fetal outcome in our state. With this background in mind, the present study was conducted to estimate serum Vitamin D levels in pregnant women with the aim of assessing the prevalence of VDD in pregnant women and its effect on expecting mother and newborn.

METHODS

This was a cross-sectional study conducted in the Department of Biochemistry in collaboration with Department of Obstetrics and Gynecology, Indira Gandhi Institute of Medical Sciences, Patna, India, during February 2022–January 2024 after due approval by the Institutional Ethics Committee.

A total of 100 pregnant females visiting antenatal clinic were recruited in the study by convenience sampling method. Informed consent was obtained from every participant. Both primigravida (pregnant for the 1st time) and multigravida (has been pregnant more than 1 time) women with singleton pregnancy were included in the study. Information about sociodemographic characteristics of the participants

such as age, residence, educational level, food preferences (vegetarian or non-vegetarian), gestational age, parity, comorbidities, and intake of food supplements were obtained.

Pregnant women with a history of any chronic medical or surgical illness or intake of drugs affecting calcium and Vitamin D metabolism were excluded from the study.

Labor and delivery details were also recorded. Newborn birth weight was recorded at birth. The APGAR score at 1 min of birth was noted.

A 5 mL of venous blood was collected from all subjects. 25(OH)D3 level was tested by chemiluminescent immunoassay in the clinical biochemistry laboratory. Based on the level of Vitamin D, subjects were classified into following three groups according to internationally accepted guidelines [20,21].

A. Vitamin D deficient group (<20 ng/mL)
B. Vitamin D insufficient group (20–30 ng/mL)
C. Vitamin D sufficient group (>30 ng/mL).

The data analysis was done using the program, the Statistical Package for the Social Sciences (SPSS for Windows, version 21.0, Chicago, SPSS Inc.). Descriptive statistics were used to characterize the study population. Categorical variables were reported as frequency and percentages while continuous variables were expressed as mean±standard deviation. $p<0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

The mean age of the study population was 26.23±3.85 years (Supplementary Table 1). Mean level of Vitamin D in the study population was 21.82±12.95 (ng/mL). Out of 100 pregnant women tested, the level of Vitamin D was found to be sufficient only in 28% (28/100) of subjects. Vitamin D level was lower than recommended in 72% (72/100) of subjects; Vitamin D was insufficient and deficient in 24% (24/100) and 48% (48/100) of the subjects, respectively. The mean period of gestation was 33.37±3.72 weeks. The mean weight of the newborn was 2.71±0.33 kg. A significant correlation was observed between newborn birth weight and serum Vitamin D level of the mother. The mean APGAR score was 7.17±1.20. APGAR score was normal (7–10) in 80% of baby delivered. It was moderately and severely depressed in 17% and 3% of babies, respectively (Table 1). The clinical and demographic characteristics of the study population are shown in Table 1.

Table 1: Clinical and demographic characteristics of the study population

Parameters	Mean±standard deviation; n (%)
Age	26.23±3.85
Vitamin D values	21.82±12.95
POG	33.37±3.72
NBWT	2.71±0.33
APGAR score	7.17±1.20
Gravida	1.66±0.69
Locality	
Urban	51 (51)
Rural	49 (49)
Mode of delivery	
Vaginal	84 (84)
Cesarean section	16 (16)
Education	
Non-matric	6 (6)
Intermediate	57 (57)
Undergraduate	19 (19)
Postgraduate	6 (6)
Matric	12 (12)
Food habit	
Vegetarian	49 (49)
Non-vegetarian	51 (51)
Low birth weight	21 (21)
Pre-eclampsia	8 (8)
APGAR category	
Normal (7–10)	80 (80)
Moderately depressed (4–6)	17 (17)
Severely depressed (0–3)	3 (3)
Vitamin D category	
Sufficient	28 (28)
Insufficient	24 (24)
Deficient	48 (48)

POG: Period of gestation, APGAR: Appearance, pulse, grimace, activity, and respiration

Vaginal delivery was observed in the majority of the subjects (84%). Majority of the subjects were pregnant for the 1st time (45/100). Gravida status of the subjects did not show any significant relation with Vitamin D level. Majority of the patients (61/100) were living in rural areas. No significant relation was observed between place of residence and Vitamin D level. Educational level of the subjects was not associated with the Vitamin D level and outcome of pregnancy. Food habits and mode of delivery did not show any significant correlation with Vitamin D level.

Pre-eclampsia was observed in 8% (8/100) of the subjects. A significant correlation was observed between occurrence of pre-eclampsia and maternal Vitamin D level, as shown in Table 2. Pre-eclampsia was also significantly associated with age and gravid status of the subjects.

LBW was seen in 21% of the subjects. LBW showed a significant relationship with maternal Vitamin D level ($p<0.001$). Association of Vitamin D status and maternal and newborn outcomes is shown in Table 3.

APGAR score was normal in all the newborns borne to the mother with sufficient level of Vitamin D while severely depressed babies were seen in the case of mothers with VDD. APGAR score was found to be significantly associated with serum Vitamin D level, as shown in (Tables 2-4).

The occurrence of VDD in pregnancy is a global problem with a large variation in prevalence rates across different populations. In this study, we found that only 28% (28/100) of the pregnant women had sufficient level of Vitamin D. In 72% of the women, Vitamin D level was found to be low. In 24% (24/100) of the pregnant women, Vitamin D level was insufficient while in 48% (48/100) of pregnant women, it was deficient. Our result is in conformity with results of studies done by others [22-24].

However, it differs from those reported by Shrestha *et al*. who reported a prevalence of VDD and insufficient Vitamin D level among pregnant women 81% (64/79) and 11.39% (9/79), respectively [25]. In a study by Marwaha *et al*., 96% of urban Indian women were Vitamin D deficient [26]. In our study, 79% (79/100) of the women delivered babies having normal birth weight (birth weight ≥2500 g). No case of LBW was seen in mother with sufficient level of Vitamin D. Among VDD mother, prevalence of LBW was 29.16% (21/72). In the present study, VDD was associated with an increased risk of low-birth-weight babies. Ravinder *et al*. in their study on south Indian women, also reported similar findings [27]. A meta-analysis by Fang *et al*. has also shown association between VDD among pregnant mothers and a higher risk of LBW [28]. Leffelaar *et al*., in their study on 3779 mothers, reported an increased rate of LBW baby in condition of deficient and insufficient Vitamin D status [29]. At present, there is no consensus to advocate routine screening for VDD in pregnancy in terms of health benefits or cost effectiveness. However, prevention of maternal VDD could be an important public measure to decrease the risk of LBW baby. Testing of pregnant women at risk rather than all pregnant women may be

Table 2: Association of Vitamin D status and maternal demographic, clinical, and newborn outcomes

Parameters	Sufficient		Insufficient		Deficient		p-value
Locality							
Urban	18	64.3%	9	37.5%	24	50.0%	0.15
Rural	10	35.7%	15	62.5%	24	50.0%	
Education							
Non-matric	0	0	1	4.2%	5	10.4%	0.38
Intermediate	18	64.3%	15	62.5%	24	50%	
Undergraduate	5	17.9%	4	16.7%	10	20.8%	
Postgraduate	3	10.7%	2	8.3%	8	16.7%	
Matric	2	7.1	2	8.3%	8	16.7%	
Food habit							
Vegetarian	15	53.6%	11	45.8%	23	47.9%	0.84
Non-vegetarian	13	46.4%	13	54.2%	25	52.1%	
Mode of delivery							
Vaginal	23	82.1%	20	83.3%	41	85.4%	0.93
Cesarean section	5	17.9%	4	16.7%	7	14.6%	
Pre-eclampsia							
Yes	0	0	0	0	8	16.7%	0.01
No	28	100%	24	100%	40	83.3%	
Low birth weight							
Yes	0	0	1	4.2%	20	41.7%	<0.001
No	28	100%	23	95.8%	28	58.3%	
APGAR							
Normal (7–10)	28	100%	24	100%	28	58.3%	<0.001
Moderately depressed (4–6)	0	0	0	0	17	35.4%	
Severely depressed (0–3)	0	0	0	0	3	6.3%	

APGAR: Appearance, pulse, grimace, activity, and respiration

Table 3: Association of Vitamin D status and maternal and newborn outcomes

Parameters	Vitamin D categories	Mean	95% confidence interval for mean		p-value
			Lower bound	Upper bound	
Age	Sufficient (n=28)	25.25±3.82	23.77	26.73	0.28
	Insufficient (n=24)	26.75±4.57	24.82	28.68	
	Deficient (n=48)	26.54±3.43	25.55	27.54	
POG	Sufficient (n=28)	31.71±4.41	30.00	33.43	0.02
	Insufficient (n=24)	33.83±3.21	32.48	35.19	
	Deficient (n=48)	34.10±3.27	33.15	35.05	
Gravida	Sufficient (n=28)	1.50±0.58	1.28	1.72	0.29
	Insufficient (n=24)	1.79±0.66	1.51	2.07	
	Deficient (n=48)	1.69±0.75	1.47	1.90	
NBWT	Sufficient (n=28)	3.01±0.30	2.8898	3.1238	<0.001
	Insufficient (n=24)	2.76±0.23	2.6605	2.8537	
	Deficient (n=48)	2.51±0.25	2.4390	2.5852	
APGAR score	Sufficient (n=28)	7.96±0.69	7.7	8.23	<0.001
	Insufficient (n=24)	7.46±0.51	7.24	7.67	
	Deficient (n=48)	6.56±1.35	6.17	6.95	

POG: Period of gestation, APGAR: Appearance, pulse, grimace, activity, and respiration

an advantageous step in preventing VDD without increasing the economic burden.

There was no significant association between Vitamin D status and mode of delivery (vaginal or cesarean section). This finding is in concordance with those reported by Gómez-Carrascosa *et al*. [30].

Several other studies also reported no significant correlation between Vitamin D level and mode of delivery [31]. Our study is in contrast with the one reported by Talukdar and Joshi who reported a significant association between VDD and an increase in the rate of primary cesarean section [22,32]. In our study, pre-eclampsia was seen in eight cases out of 100 women tested for Vitamin D level. VDD was present in all cases of pre-eclampsia showing a significant correlation between VDD and pre-eclampsia. Tammo and Yıldız, in their study, showed that pre-eclampsia could be present in cases with Vitamin D insufficiency and VDD [33].

Sharma *et al*., in their study done on women in North-Eastern that Vitamin D level, have very low in pre-eclamptic women compared to normotensive women [34]. Our finding correlates well with other studies which reported increased risk of pre-eclampsia in mothers with low level of vitamin D [35-37].

In our study, it was observed that there was a higher prevalence of low APGAR score in babies born to mothers with low Vitamin D level. VDD was significantly associated with lower APGAR score. Our finding correlates well with other studies [18,33]. However, it differs from some other authors who reported no significant association between the Vitamin D level of the mother and the APGAR score of the newborn [16].

Our study has some limitations which must be taken into consideration for future research work. Our study was limited by a small sample size. Furthermore, the study was conducted at a tertiary care center which caters mainly to the referred patients. Our sample size may not be truly

Table 4: Correlation between Vitamin D levels and maternal and newborn outcomes

Correlations	Age	Vitamin D values	POG	NBWT	APGAR score at 1 min	Gravida
Age						
Pearson Correlation	1	−0.111	0.150	−0.127	−0.017	0.570**
Sig. (two-tailed)		0.273	0.135	0.209	0.864	<0.001
N	100	100	100	100	100	100
Vitamin D values						
Pearson Correlation	−0.111	1	−0.238*	0.738**	0.616**	−0.088
Sig. (two-tailed)	0.273		0.017	<0.001	<0.001	0.382
N	100	100	100	100	100	100
POG						
Pearson Correlation	0.150	−0.238*	1	−0.253*	−0.155	0.101
Sig. (two-tailed)	0.135	0.017		0.011	0.125	0.316
N	100	100	100	100	100	100
NBWT						
Pearson Correlation	−0.127	0.738**	−0.253*	1	0.655**	−0.041
Sig. (two-tailed)	0.209	<0.001	0.011		<0.001	0.688
N	100	100	100	100	100	100
APGAR score at 1 min						
Pearson Correlation	−0.017	0.616**	−0.155	0.655**	1	0.034
Sig. (two-tailed)	0.864	<0.001	0.125	<0.001		0.735
N	100	100	100	100	100	100
Gravida						
Pearson Correlation	0.570**	−0.088	0.101	−0.041	0.034	1
Sig. (two-tailed)	<0.001	0.382	0.316	0.688	0.735	
N	100	100	100	100	100	100

**Correlation is significant at the 0.01 level (two-tailed), *Correlation is significant at the 0.05 level (two-tailed), POG: Period of gestation, APGAR: Appearance, pulse, grimace, activity, and respiration

representative of the general population. Hence, the findings of the present study may not be generalized to the whole population.

CONCLUSION

VDD remains a major public health problem. There is a very high prevalence of VDD in pregnant women of both rural and urban areas. VDD in pregnancy is associated with several complications to the expectant mother as well as the fetus. These complications have implications not only on the maternal and neonatal morbidity and mortality but also on the future health of the mother and child. Complications such as pre-eclampsia, LBW babies, and low APGAR score were observed in the present study. There is a need of extensive clinical research on the impact of VDD in pregnancy on mother and fetal health. Multi-centric studies involving a larger population from different regions and ethnicity, assessment of several effects on pregnancy, and further impact on future health of both mother and child are the need of hour.

AUTHORS CONTRIBUTIONS

Dr. Usha Kumari-Origin of concept, Development of research proposal, Doing experiments.

Dr. Raj Kishor Sharma-Manuscript writing, Result interpretation, Statistical analysis.

Dr. Archana Sinha- Recruitment of patients, Antenatal care and treatment of pregnant women.

ETHICAL CONSIDERATIONS

Ethical clearance was obtained from the Institutional Ethics Committee.

CONFLICTS OF INTEREST

No conflicts.

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Nil.

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SUPPLEMENTARY TABLE

Supplementary Table 1

Parameters	Food habit	n	Mean±SD		p-value
Vitamin D values	Vegetarian	49	21.41±12.44		0.75
	Non-vegetarian	51	22.23±13.54		
POG	Vegetarian	49	32.71±4.1		0.08
	Non-vegetarian	51	34.00±3.24		
NBWT	Vegetarian	49	2.69±0.35		0.61
	Non-vegetarian	51	2.73±0.32		
APGAR Score	Vegetarian	49	7.96±0.69		0.005
	Non-vegetarian	51	7.46±0.51		
Parameters	**Pre-eclampsia**	**n**	**Mean±SD**		**p-value**
Age	Yes	8	30.13±3.36		0.002
	No	92	25.89±3.71		
Gravida	Yes	8	2.25±1.04		0.01
	No	92	1.61±0.63		
Vitamin D values	Yes	8	7.53±3.81		<0.001
	No	92	23.06±12.72		
POG	Yes	8	34.75±2.38		0.28
	No	92	33.25±3.81		
NBWT	Yes	8	2.50±0.38		0.07
	No	92	2.73±0.32		
APGAR Score	Yes	8	5.88±1.73		0.001
	No	92	7.28±1.08		
Parameters	**APGAR Cat**	**n**	**Mean**	**Standard Deviation**	**p-value**
Age	1.00	80	26.24	4.085	0.99
	2.00	17	26.24	2.884	
Gravida	1.00	80	1.70	0.683	0.36
	2.00	17	1.53	0.717	
Vitamin D values	1.00	80	25.364	11.9334	<0.001
	2.00	17	8.188	4.3866	
POG	1.00	80	32.94	3.833	0.22
	2.00	17	35.24	2.818	
NBWT	1.00	80	2.8155	0.27801	<0.001
	2.00	17	2.3200	0.13181	
Parameters	**LBW**	**n**	**Mean**		**p-value**
APGAR score at 1 min	Yes	21	5.71±1.52		<0.001
	No	79	7.56±0.71		
Age	Yes	21	25.90±2.51		0.67
	No	79	26.32±4.14		
Gravida	Yes	21	1.48±0.68		0.17
	No	79	1.71±0.68		
Vitamin D values	Yes	21	7.61±4.41		<0.001
	No	79	25.61±11.81		
POG	Yes	21	34.81±3.09		0.04
	No	79	32.99±3.80		