Section: Pediatrics

Original Research Article

TO STUDY THE ASSOCIATION BETWEEN MATERNAL VITAMIN D DEFICIENCY DURING THIRD TRIMESTER OF PREGNANCY AND THE RISK OF HAVING SMALL FOR GESTATIONAL AGE INFANTS IN INDIAN POPULATION

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Abstract

Background: The present study was to study the association between maternal vitamin D deficiency during third trimester of pregnancy and the risk of having Small for Gestational Age infants in Indian population. **Materials and Methods:** A Prospective Observational Study was carried out in the department of obstetrics and Gynecology and department of pediatrics Hospital. A total of 84 numbers of pregnant women with singleton pregnancy, attending OPD and admitted in OBG department and their newborns were recruited for the study over a period of 6 months. **Result :**Out of total 84 women; 4 (4.76%) was observed to have Severe deficient level; 56 (66.67%) Deficient level; 18 (21.43%) Insufficient level; 5 (5.95%) Sufficient level and 1 (1.19%) woman was observed to have “Excess level” of Vitamin D. Out of total 84 babies; 14 (16.67%) baby was SGA. Overall, P value was 0.834, which showed that maternal vitamin D level has no statistically significant relationship with head circumference of the baby. Out of total 84 babies; 12 (14.29%) baby was Low birth weight [LBW]. Overall, P value was 0.628, which showed that maternal vitamin D level has no statistically significant relationship with LBW of the baby. In 3 (3.57%) women, birth weight of baby was < 3rd centile; in 11 (13.10%) women birth weight was < 10rd centile; in 53 (63.10%) women, birth weight was between 10-50th centile; in 15 (17.86%) women, birth weight was between 51-90th centile and in 2 (2.38%) women, birth weight was between 91-97th centile. **Conclusion:**We remained uncertain about the association of maternal vitamin D deficiency with increased risk of adverse effects on maternal and neonatal outcome. Several studies explored the association between maternal vitamin D status during pregnancy and its effect on maternal and neonatal outcome with contradictory results. Research from developing countries is very limited. Our study also has contradictory results. Since we recruited only 84 subjects in our study, more large-scale studies are required to find out the exact effects of hypovitaminosis D during pregnancy on neonatal outcomes.

INTRODUCTION

Colorectal cancer (CRC) is the fourth most prevalent cancer in the United States.[1] Evidence strongly suggests that making healthful dietary changes may influence the risk of recurrence and/or the development of second primary tumors in CRC survivors.[2] Although evidence indicates that cancer survivors are motivated to make positive changes in diet.[3,4] Good reproductive health and pregnancy outcome depend upon a woman’s nutrition before and during pregnancy.[5] Experts suggest that the optimal supply of micronutrients (folic acid, calcium, iron, vitamin D) is important for optimal pregnancy outcomes.[5]

The deficiency of micronutrients results in abnormal development of fetoplacental unit leading to a spectrum of adverse pregnancy outcomes.[6] Vitamin D inadequacy is thought to cause many gestation-associated disorders like preeclampsia, gestational diabetes, premature rupture of membrane, preterm birth, stillbirth, neonatal death, small for gestational age, low birth weight, etc.[7] Among these, previous studies linking vitamin D deficiency with preeclampsia, have many lacunas like small study population due to which this association is yet to be established by a study with a large sample size. It is necessary to establish this association by a properly designed study so that its detrimental impacts on pregnancy can have a preventive approach by supplementing an adequate dose of vitamin D.[7]

Vitamin D deficiency recognized as a burning problem in recent era globally has become a rising threat to modern-day obstetrics with an estimated incidence of 22.7–90.7 % in pregnant women worldwide.[7]Sacchan et al,[8] in their study, found 84.3 % of urban and 83.6 % of rural women have vitamin D deficiency in (Lucknow) northern part of India, despite being a tropical country. The United States Institute of Medicine has defined the level of vitamin D of more than 20 ng/ml to be normal level for pregnant women.[9] According to the US endocrine society, serum vitamin D level of 30 ng/ml or more is considered normal during pregnancy.[10] Moreover, the US endocrine society has classified the vitamin D levels as follows.[10] Besides maintaining bone health through calciotropism, vitamin D is also said to play a central role in cellular proliferation and differentiation, vascular functions, and immune system regulation.[11]

The present study was to study the association between maternal vitamin D deficiency during third trimester of pregnancy and the risk of having Small for Gestational Age infants in Indian population.

MATERIALS AND METHODS

A Prospective Observational Study was carried out in the department of obstetrics and Gynecology and department of pediatrics Hospital. A total of 84 numbers of pregnant women with singleton pregnancy, attending OPD and admitted in OBG department and their newborns were recruited for the study over a period of 6 months.

Pregnant women, who were advised for serum 25 (OH) D levels, based on clinically suspected vitamin D deficiency, by Gynecologist and also those pregnant women, who were willing to participate in the study, voluntarily were included in the study and subjected to testing serum 25 (OH) D levels at or after 36 weeks, after informed written consent. Fluorescence Immunoassay (FIA) method was used to assess the Vitamin D status. Neonatal outcomes including small for gestational Age, Birth Weight, Length and Head size were studied. Detailed history including complete demographic details, dietary history, past medical history, present obstetric history, antenatal history including details of any antenatal complications, intake of multivitamin, vitamin D, and calcium tablets during pregnancy, its dose, and duration; and socio-economic history were recorded from the recruited pregnant women using a close ended questionnaire. Patients were followed up for labor and delivery details including induction of labor, mode of delivery (normal VD/Assisted VD/LSCS), indication of LSCS, any complications; Neonatal characteristics in terms of gestational age at delivery, anthropometry (birth weight, height and head circumference) to know SGA and LBW infants, sex, APGAR score, any congenital anomaly or NICU admission were recorded; and it was statistically compared with the outcome in pregnant women having sufficient level of vitamin D. Data was collected through specially designed proforma after explaining and taking verbal consent. There is no consensus in defining hypovitaminosis D in pregnancy and cutoff serum value range from 10 to 32 ng/ml. According to American College of Obstetrics and Gynecology (ACOG), serum 25(OH) D concentration of at least 20 ng/ml is needed to avoid bone problems and vitamin D deficiency should be defined as circulating 25 (OH) D levels level less than 32 ng/ml (39). According to Canadian PaediatricSociety, serum 25 (OH) D concentrations below10 ng/ml are used as a cutoff for deficiency and between 10 and 30 ng/ml as a cut off for insufficiency.[12]

For detailed statistical analysis, I had divided the mothers, into five groups depending upon their vitamin D levels:

Severe deficient: Vitamin D level <4ng/ml
Deficient: Vitamin D level <20ng/ml
Insufficient: Vitamin D level 20-30ng/ml
Sufficient: Vitamin D level 31-70ng/ml
Excess/toxic: Vitamin D level >70ng/ml

Inclusion Criteria

Pregnant women, with singleton pregnancy of Gestational age at 36 weeks or more, who were advised for serum 25 (OH) D level, based on clinically suspected vitamin D deficiency, by Gynecologist and also those pregnant women who were willing to participate in the study, voluntarily.

Exclusion Criteria

Known risk factor of Small for Gestational Age, like cardiovascular disease, hypertension, diabetes mellitus, placenta praevia, anemia. Preexisting parathyroid condition. Renal disease Hepatic disease Musculoskeletal disorder Not willing to participate in the study.

Statistical analysis: Categorical variables were presented in number and percentage (%) and continuous variables will be presented as mean ± SD and median. Normality of data was tested by Kolmogorov-Smirnov test. If the normality is rejected then non parametric test was used.

RESULTS

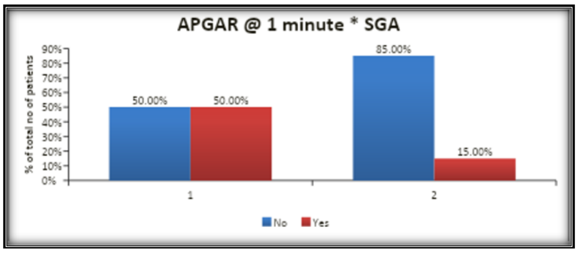

Figure 1: APGAR score @1 minute

<7 APGAR score at 1 minute was observed in 4 (4.76%) baby, among them 2 (50%) baby was SGA. =>7 APGAR score at 1 minute was observed in 80 (95.24%) baby; among them 12 (15%) baby was SGA. P value was 0.128, which showed that APGAR score @ 1 minute has no statistically significant relationship with SGA of the baby.

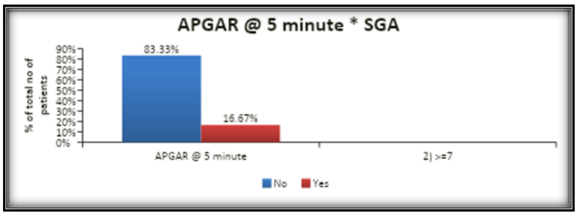

Figure 2: APGAR score @ 5 minutes

>=7 APGAR score at 5 minute was observed in all women. 16.67% baby was SGA.

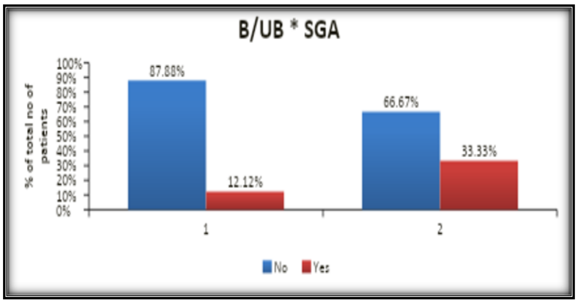

Figure 3: DEMOGRAPHIC DETAILS SGA BABY

66 (78.57%) women were Booked case and 18 (21.43%) was Un-booked case. Among Booked women, 12.12% baby was SGA; whereas among Un-booked women, 33.33% baby was SGA. P value was 0.032, which showed that booked status of mother has no statistically significant relationship with small for gestational age of the baby.

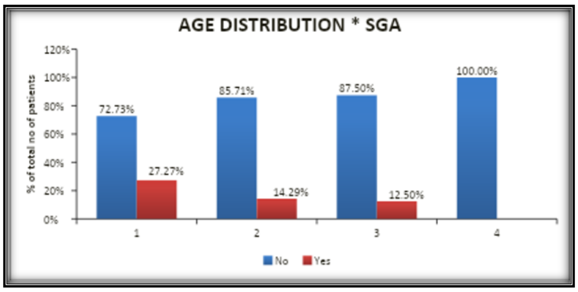

Figure 4: Age distribution SGA

Percentage of women between ages 21-25 year was 26.19%; between 26-30 years was 50%; between 31-35 years was 19.05% and above 35 years was 4.76%. In women between 21-25 year of age, 27.27% baby was SGA. In women between 26-30 year of age, 14.29% baby was SGA. In women between 31-35 year of age, 12.50% baby was SGA, whereas in pregnant women >35 year of age, no baby was SGA.

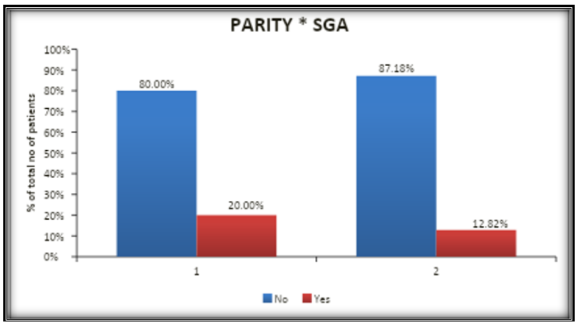

Figure 5: Parity distribution

53.57% was primigravida and 46.43% was multigravida. In primigravida, 20% baby was SGA; whereas in multigravida 16.67% was SGA.

Table 1: vitamin d level among pregnant women.

	Percentage
Severe deficient	4 (4.76%)
Deficient	56 (66.67%)
Insufficient	18 (21.43%)
Sufficient	5 (5.95%)
Excess	1 (1.19%)
Total	84 (100%)

Table 2: vitamin D [NG/ML] of women SGA baby

		SGA		**P value**	**P value**
		No	**Yes**		
VITD[NG/ML]	SevereDeficient	3 (75%)	1 (25%)	0.525	0.834
	Deficient	46 (82.14%)	10 (17.86%)	0.765	
	Insufficient	15 (83.33%)	3 (16.67%)	1.000	
	Sufficient	5 (100%)	0	0.584	
	Excess	1 (100%)	0	1.000	
Total		70 (83.33%)	14 (16.67%)		

Table 3: VIT D [NG/ML] OF WOMEN LOW BIRTH WEIGHT [LBW] BABY

		Low birth weight		**P value**	**P value**
		No	**Yes**		
VITD[NG/ML]	Severe deficient	4 (100%)	0	1	0.628
	Deficient	48 (85.71%)	8 (14.29%)	1	
	Insufficient	14 (77.78%)	4 (22.22%)	0.276	

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	Sufficient	5 (100%)	0	1	
	Excess	1 (100%)	0	1	
Total		72 (85.71%)	12 (14.29%)		

Table 4: VIT D [NG/ML] of women weight centile of baby

		WT CENTILE						P value
		1) <3centile	2) <10centile	3) 10-50centile	4) 51-90centile	5)91-97centile	P-value	
VITD [NG/ML]	Severe deficient	0	1 (25%)	2 (50%)	1 (25%)	0	0.919	0.744
	Deficient	3(5.36%)	7(12.5%)	34(60.71%)	11(19.64%)	1(1.79%)	0.691	
	Insufficient	0	3(16.67%)	12(66.67%)	3(16.67%)	0	0.800	
	Sufficient	0	0	4 (80%)	0	1(20%)	0.061	
	Excess	0	0	1(100%)	0	0	0.964	
Total		3(3.57%)	11(13.10%)	53(63.10%)	15(17.86%)	2(2.38%)		

Table 5: VIT D [NG/ML] of women length centile of baby

		LENGTH CENTILE					Pvalue	P value
		1) <3centile	3) 10-50centile	4) 51-90centile	5) 91-97centile	6) >97centile		
VITD [NG/ML]	Severe deficient	0	0	4 (100%)	0	0	0.558	0.817
	Deficient	1(1.79%)	18(32.14%)	30(53.57%)	5(8.93%)	2(3.57%)	0.626	
	Insufficient	0	4(22.22%)	11(61.11%)	3(16.67%)	0	0.632	
	Sufficient	0	1(20.00%)	3 (60%)	0	1(20%)	0.320	
	Excess	0	0	1 (100%)	0	0	0.948	
Total		1(1.19%)	23(27.38%)	49(58.33%)	8(9.52%)	3(3.57%)		

Table 6: VIT D [NG/ML] of women lga baby

		LGA		P value	P value
		No	Yes		
VITD [NG/ML]	Severe deficient	4 (100%)	0	1	0.120
	Deficient	55 (98.21%)	1 (1.79%)	1	
	Insufficient	18 (100%)	0	1	
	Sufficient	4 (80%)	1 (20%)	0.116	
	Excess	1 (100%)	0	1	
Total		82 (97.62%)	2 (2.38%)		

Out of total 84 women; 4 (4.76%) was observed to have Severe deficient level; 56 (66.67%) Deficient level; 18 (21.43%) Insufficient level; 5 (5.95%) Sufficient level and 1 (1.19%) woman was observed to have “Excess level” of Vitamin D. [Table 1]

Out of total 84 babies; 14 (16.67%) baby was SGA. Overall, P value was 0.834, which showed that maternal vitamin D level has no statistically significant relationship with head circumference of the baby. [Table 2]

Out of total 84 babies; 12 (14.29%) baby was Low birth weight [LBW]. Overall, P value was 0.628, which showed that maternal vitamin D level has no statistically significant relationship with LBW of the baby. [Table 3]

In 3 (3.57%) women, birth weight of baby was < 3rd centile; in 11 (13.10%) women birth weight was < 10rd centile; in 53 (63.10%) women, birth weight was between 10-50th centile; in 15 (17.86%) women, birth weight was between 51-90th centile and in 2 (2.38%) women, birth weight was between 91-97th centile. Overall, P value was 0.744, which showed that maternal Vitamin D level has no statistically significant relationship with birth weight of the baby. [Table 4]

In 1 (1.19%) women, birth length of baby was < 3rd centile; in 23 (27.38%) women, birth length was between 10-50th centile; in 49 (58.33%) women, birth length was between 51-90th centile; in 8 (9.52%) women, birth length was between 91-97th centile and in 3 (3.57%) women, birth length of baby was >97th centile. Overall, P value was 0.817, which showed that maternal Vitamin D level has no statistically significant relationship with birth length of the baby. [Table 5]

Out of total 84 babies; 2 (2.38%) baby was LGA. Overall, P value was 0.120, which showed that maternal vitamin D level has no statistically significant relationship with LGA of the baby. [Table 6]

DISCUSSION

Vitamin D deficiency is a significant public health problem in both developed and developing countries including India. Although India is a tropical country with abundant sunshine; still vitamin D deficiency is very common in all age groups and both sexes across the country. Vitamin D deficiency is recognized as the most untreated nutritional deficiency currently in the world.[13] There is growing concern about health consequences of high prevalence of vitamin D deficiency [VDD] in pregnancy worldwide with up to 50% of pregnant women classified as vitamin D deficient.[14] Despite sufficient and stable sunny conditions across equatorial countries, studies have reported high

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prevalence of VDD in pregnant and lactating women and infants in such areas, ranging from 26–95% during pregnancy.[15]

Out of total 84 women; 4 (4.76%) was observed to have Severe deficient level; 56 (66.67%) Deficient level; 18 (21.43%) Insufficient level; 5 (5.95%) Sufficient level and 1 (1.19%) woman was observed to have "Excess level" of Vitamin D. Out of total 84 babies; 14 (16.67%) baby was SGA. Overall, P value was 0.834, which showed that maternal vitamin D level has no statistically significant relationship with head circumference of the baby. Out of total 84 babies; 12 (14.29%) baby was Low birth weight [LBW]. There are few randomized trials of maternal vitamin D supplementation, and we identified two that studied pathologic infant growth.[16,17] In 126 Asian women living in Britain, daily 1000 IU in the third trimester compared to placebo reduced risk of SGA by 13%, although this difference was not statistically significant (0.05 < P < 0.10).16 In another British population (n=179), no effect of daily 800 IU or a large single dose of 200,000 IU at 27 weeks compared to no treatment was observed.[17] This trial was not placebo controlled. A recent Cochrane review reported that there is limited evidence to assess the impact of vitamin D supplementation on SGA.[18]

Overall, P value was 0.628, which showed that maternal vitamin D level has no statistically significant relationship with LBW of the baby. In 3 (3.57%) women, birth weight of baby was < 3rd centile; in 11 (13.10%) women birth weight was < 10rd centile; in 53 (63.10%) women, birth weight was between 10-50th centile; in 15 (17.86%) women, birth weight was between 51-90th centile and in 2 (2.38%) women, birth weight was between 91-97th centile. Overall, P value was 0.744, which showed that maternal Vitamin D level has no statistically significant relationship with birth weight of the baby. In 1 (1.19%) women, birth length of baby was < 3rd centile; in 23 (27.38%) women, birth length was between 10-50th centile; in 49 (58.33%) women, birth length was between 51-90th centile; in 8 (9.52%) women, birth length was between 91-97th centile and in 3 (3.57%) women, birth length of baby was >97th centile. Overall, P value was 0.817, which showed that maternal Vitamin D level has no statistically significant relationship with birth length of the baby. Two smaller studies, one in a general obstetric population,[19] and one in women at high risk for preeclampsia,[20] found no association between SGA and vitamin D status but were likely underpowered with only 46 and 13 cases of SGA, respectively.

Out of total 84 babies; 2 (2.38%) baby was LGA. Overall, P value was 0.120, which showed that maternal vitamin D level has no statistically significant relationship with LGA of the baby. >=7 APGAR score at 5 minute was observed in all women. 16.67% baby was SGA. 66 (78.57%) women were Booked case and 18 (21.43%) was Un-booked case. Among Booked women, 12.12% baby was SGA; whereas among Un-booked women, 33.33% baby was SGA. P value was 0.032, which showed that booked status of mother has no statistically significant relationship with small for gestational age of the baby. Percentage of women between ages 21-25 year was 26.19%; between 26-30 years was 50%; between 31-35 years was 19.05% and above 35 years was 4.76%. In women between 21-25 year of age, 27.27% baby was SGA. In women between 26-30 year of age, 14.29% baby was SGA. In women between 31-35 year of age, 12.50% baby was SGA, whereas in pregnant women >35 year of age, no baby was SGA. 53.57% was primigravida and 46.43% was multigravida. In primigravida, 20% baby was SGA; whereas in multigravida 16.67% was SGA. A plausible mechanism for the impact of maternal vitamin D on fetal growth is placental vascularization, which has received considerable attention in its association with fetalgrowth.[21-23]

CONCLUSION

We remained uncertain about the association of maternal vitamin D deficiency with increased risk of adverse effects on maternal and neonatal outcome. Several studies explored the association between maternal vitamin D status during pregnancy and its effect on maternal and neonatal outcome with contradictory results. Research from developing countries is very limited. Our study also has contradictory results. Since we recruited only 84 subjects in our study, more large-scale studies are required to find out the exact effects of hypovitaminosis D during pregnancy on neonatal outcomes.

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