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Original Research Article

Study of Association Between Maternal 25 – hydroxy Vitamin D_3 Level and Neonatal Outcome

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Abstract: The widespread global prevalence of hypovitaminosis D during pregnancy and its implications for undesirable health outcomes in present and future generations is an area of growing concerns. The study was undertaken with an aim to determine vitamin D status among pregnant women and their new-borns and to find association between maternal vitamin D level during pregnancy and neonatal outcome. This hospital based, observational study was conducted on 250 pregnant patients and their new-borns in departments of Obstetrics & Gynaecology and Paediatrics at SMS Medical College, Jaipur from May 2014 to April 2015. Maternal and cord blood samples were drawn at the time of delivery for 25-hydroxy vitamin D, S. calcium, S. phosphorus and S. ALP levels estimation. 86% of women were vitamin D deficient, 12.4% insufficient and only 1.6% had sufficient vitamin D levels. Their new born also showed similar results. Mean neonatal vitamin D level in vitamin D deficient , insufficient , sufficient mothers were 5.73 ± 2.7 ng/ml, 17.77 ± 9.62 ng/ml and 33.09 ± 5.22 ng/ml respectively. Maternal and cord blood vitamin D levels showed significant positive correlation ($r = 0.90$, P value < 0.001). Maternal Vitamin D status was not significantly associated with neonatal biochemical parameters (S. calcium, S. phosphorus and S. ALP levels) and anthropometry. The strong correlation between 25(OH) D concentrations in mothers and their new-borns indicate that adequate vitamin D intake for mothers should be emphasized through maternal supplementation which would achieve the double effect of preventing vitamin D deficiency in both mothers and children.
Keywords: Vitamin D, Vitamin D Deficiency, Neonates, S. Calcium levels

INTRODUCTION

Vitamin D deficiency is an old public health problem. Despite the numerous preventive and therapeutic strategies now available including supplements and foods that contain natural or added vitamin D, its deficiency has surfaced as a global health problem [1-3].

Maternal Vitamin D deficiency has been related to adverse effects on foetal and neonatal growth and bone development[4,5]. The significance of maternal deficiency during pregnancy is that the fetus is developing in a state of hypovitaminosis D, which likely has significant effects on innate immune function and fetal and childhood bone and physical development[6,7,8].

MATERIAL & METHODS

The study was undertaken to study the magnitude of vitamin D deficiency among pregnant women of the state of Rajasthan and to find association of maternal vitamin D status with socio-demographic factors and its effect on neonatal biochemical parameters (Vitamin D levels, S. Calcium, Phosphorus and Alkaline Phosphatase) and anthropometry.

This descriptive and observational study was done on 250 pregnant patients in department of Obstetrics and Gynaecology and Pediatrics, SMS Medical College Jaipur from June 2014 to April 2015. All healthy pregnant women with singleton pregnancies and their full term new-borns with prior consent were included in the study. Pregnant mothers with chronic medical illness and mothers with complicated pregnancy (APH, PIH, preeclampsia, GDM, Preterm, Twin pregnancy) were excluded from study. Prior permission was taken from the ethical committee of the hospital.

A detailed history was taken regarding obstetric history, sociodemographic data, dietary habits, lifestyle, and calcium or vitamin D supplements during pregnancy.

Mode of delivery, gestational age at birth, anthropometric measurements of new born within 24 – 48 hours were noted (head circumference & length to nearest 1mm and weight to the nearest 10 gm). SGA was defined as live – born infants with <10th percentile of birth weight according to normograms based on gender and gestational age.

Maternal venous blood and cord blood sample of the new born was taken at the time of delivery for 25 hydroxy vitamin D (25- OH D), S. Calcium, S. Phosphorus and S. ALP levels estimation.

Serum level of 25-OH vitamin D, a vitamin D metabolite, was measured using a commercially available kit after extraction using immunodiagnostic enzyme assay (EIA) using ADVIA Centaur Vitamin D assay kits from Siemens Diagnostics. All biochemical tests were performed in biochemistry department, S.M.S Hospital, Jaipur.

Subjects were classified into three categories: [9]

- Vitamin D Deficient - 25(OH) D < 10ng/ml (<25nmol/l)
- Vitamin D Insufficient - 25(OH)D 10 – 29ng/ml (25 – 74.9nmol/l)
- Vitamin D Sufficient - 25(OH)D >30ng/ml (≥75nmol/l)

Student T-test was used to compare the difference between means variables. Proportions were compared using the chi – square test. Pearson's correlation coefficient was used for correlations. Two – tailed significance at P<0.05 was considered as significant.

RESULTS

The mean age of study population was 24 years. In our study, Vitamin D deficiency was found significantly more in pregnant women aged< 30 years compared to those more than 30 years (P value <0.001). There was no significant association between maternal vitamin D levels and residence, religion, social status, booking status, dietary habits, gravida status or antenatal calcium and vitamin D supplement intake of pregnant women (Table 1).

86% of women were vitamin D deficient, 12.4% insufficient and only 1.6% had sufficient vitamin D levels. Their new born also showed almost similar results - 81.6% were vitamin D deficient, 15.2% insufficient and 3.2% had sufficient vitamin D levels.

Table 1: Maternal Vitamin D status according to Socio – Demographic Profile of mothers

Socio – demographic profile of mothers		Maternal Vitamin D status (ng/ml)			total	P – value
		< 10 (215)	10 – 29 (31)	≥ 30 (4)		
Age of mother	Age <30	86.8% (199)	11.7% (27)	1.3% (3)	229	P<0.001
	Age >30	76%(16)	19% (4)	4.7% (1)	21	
Residence	Rural	85% (58)	13% (9)	2% (1)	68	P=0.967
	Urban	86.2% (157)	12% (22)	1.6% (3)	182	
Religion	Hindu	87% (174)	11.5%(23)	1.5%(3)	200	P= 0.66
	Muslim	82%(41)	16%(8)	2%(1)	50	
Antenatal care status	Booked	84.5% (186)	13.6% (30)	1.8% (4)	220	P = 0.196
	Unbooked	96.6% (29)	3.3% (1)	0	30	
Gravidity	Gravida 1	83.5% (81)	14.4% (14)	2% (2)	97	P = 0.65
	≥2	87.5% (134)	11.1% (17)	1.3% (2)	153	
Maternal dietary habits	Non – vegetarian	84.6% (77)	14. 2% (13)	1% (1)	91	P = 0.716
	Vegetarian	86.7% (138)	11.3% (18)	1.8% (3)	159	
Antenatal Calcium - Vit. D Supplements	Not taken	87% (102)	13% (15)	0	117	P = 0.166
	Taken	85% (113)	12% (16)	3% (4)	133	
Socioeconomic status	Lower	46.06% (99)	35.48% (11)	50% (2)	112	P = 0.361
	Middle	46.9% (101)	48.4% (15)	25% (1)	117	
	Upper	6.9% (15)	16.1% (5)	25% (1)	21	

The mean maternal Vitamin D level was 6.84±5.86 ng/ml. The mean cord blood Vitamin D level in new-borns was 7.6±6.6 ng/ml with approximately 97% new-borns having deficient or insufficient Vitamin D levels. Maternal and cord blood vitamin D levels showed significant positive correlation (r = 0.90, P value < 0.01). Maternal Vitamin D status also showed positive correlation with cord blood serum calcium levels (r = 0.174, p = 0.006). However there was no significant correlation with cord blood S. ALP levels (r = − 0.099, p value = 0.12) or S.PO_4 (r = 0.034, p =0.587). (Table 2)

Cord blood Vitamin D levels were significantly lower in pregnant women with deficient Vitamin D levels (5.73 ± 2.7 ng/ml) compared to those with insufficient or sufficient Vitamin D levels (17.77 ± 9.62 ng/ml and 33.09 ± 5.22 ng/ml respectively) (p value<0.01). Neonatal Serum calcium, S. PO_4 , S. ALP levels did not differ significantly in relation to maternal vitamin D status. (Table 3)

Mean birth weight, length and head circumference of newborn in vitamin D deficient mothers was 2.94±1.7 kg, 49.6±0.9 cm and 33.4±1.0 cm respectively, 2.78±0.4 kg, 49.5±0.9 cm and 33.2±1.0 cm respectively in vitamin D insufficient mothers and 2.9±0.4 kg, 50±0.8 cm and 32.6±1.4 cm respectively in vitamin D sufficient mothers.In our study, maternal vitamin D status did not significantly affect neonatal anthropometry (Table 4). 23.7% of the vitamin D deficient mothers and 35.4% of the vitamin D insufficient mothers had SGA babies. No mother with sufficient vitamin D level had SGA infant. However, this was not statistically significant.

Table 2: Correlation between mean maternal Vitamin D and various mean neonatal Serum parameters(S. Vitamin D, S. Calcium , S. Phosphorus, S. Alkaline Phosphatase)

Maternal Vitamin D (ng/ml) (6.84±5.86)	Mean	SD	R	Sig F change
Neonatal S. Vitamin D (ng/ml)	7.66	6.64	0.904	0.0
Neonatal S. Calcium (mg/dl)	9.23	0.93	0.174	0.006
Neonatal S.Phosphorus (mg/dl)	9.41	3.74	0.034	0.587
Neonatal S Alkaline Phosphatase (IU/L)	159.88	55.47	− 0.09	0.120

Table 3: Comparison between neonatal Vitamin D, S. Calcium, S. Alkaline Phosphatase, S. Phosphorus levels and maternal vitamin D status

Mean neonatal biochemical parameters	Maternal Vitamin D status (ng/ml)			P – value
	< 10 (215)	10 – 29 (31)	≥ 30 (4)	
Vitamin D (ng/ml)	5.73±2.70	17.77±9.62	33.09±5.22	<0.001
S. Calcium (mg/dl)	9.18±0.92	9.60±0.91	9.45±0.61	0.05
S. Phosphorus (mg/dl)	9.41±3.72	9.18±3.41	11.09±7.45	0.062
S. Alkaline Phosphatase (IU/L)	161.20±53.82	151.06±68.46	157.25±30.47	0.635

Table 4: Comparison between maternal vitamin D status and neonatal Anthropometry

Neonatal anthropometry	Maternal Vitamin D status (ng/ml)			P – value
	< 10 (215)	10 – 29 (31)	≥ 30 (4)	
Mean birth weight (kg)	2.94 ± 1.76	2.78± 0.40	2.90 ± 0.45	0.888
Mean length (cm)	49.61±0.96	49.52±0.89	50.00±0.82	0.615
Mean head circumference (cm)	33.44±1.07	33.29±1.06	32.63±1.49	0.259
Weight for gestational age:				
Small	23.7% (51)	35.4% (11)	0	
Appropriate	76.2% (164)	64.5% (20)	100% (4)	0.100

DISCUSSION

Our study revealed very high prevalence of Vitamin D deficiency in pregnant women and their new borns with almost 98% pregnant women having insufficient to severely deficient Vitamin D levels which also reflected in their new borns. This strong correlation between maternal and neonatal Vitamin D levels has been elucidated by multiple studies throughout the world [3, 6, 14-18, 23-25]. This highlights the importance of adequate Vitamin D intake for mothers during pregnancy to protect their new borns from the ill-effects of hypo vitaminosis D.

Young pregnant women (<30 yr) had significant lower Vitamin D levels as compared to pregnant women more than 30 years (p<0.001). This was also observed by Bener, *et al.;* [10] where the risk of vitamin D deficiency was higher among young pregnant women below 30 years old and Bowyer, et al.[11] in Australia where younger maternal age was associated with lower maternal serum 25-OHD (≤ 25 nmol/l) [(OR, 95% CI) 0·93 (0·89–0·97, *P* = 0·001)]. However, Maghbooli, *et al.;* [16] and El koumi, *et al.;* [23] found no significant correlation between maternal serum vitamin D concentration with age (P = 0.2).

Maternal Vitamin D levels were unrelated to residence, religion or social class. This is in accordance with Sachan *et al.;* [12], Jani *et al.;* [19] and Kalra *et al.;* [17] who reported that maternal plasma concentrations of 25(OH)D3 did not differ according to maternal social class or education level, but is in contrast to the study by Djisktra [24] and El Koumi [23] in which women with low socioeconomic state were significantly more likely to have lower 25(OH)D3 concentrations compared to those with higher socioeconomic state (p<0.05). The difference could be due to differences in population characteristics and geographical factors.

Dietary habits and supplement intake did not significantly affect maternal vitamin D status in our study despite the numerous preventive and therapeutic strategies. This is consistent with the observations from all over the world, even with those in developed countries [13-15] probably because dietary sources contribute little to vitamin D requirement of the body.

Maternal serum vitamin D status showed significant positive correlation with cord blood serum calcium levels (r=0.174, p=0.006). However, there was no significant correlation with cord blood ALP (r = -0.099, p value = 0.12) or S.PO4 (r = 0.034, p = 0.587).

In a study by El koumi, *et al.;* [23], maternal serum 25(OH) D3 strongly correlated with cord blood serum PO4 levels (r=0.83, p=0.01) and a significantly negative correlation with ALP (r= -0.78, p=0.01) but no correlation with calcium levels. Maghbooli, *et al.;* [16] also found no correlation between serum vitamin D concentrations and calcium, in contrast to our study.

According to our study, maternal Vitamin D status did not affect neonatal anthropometry. Similar observations were made by Maghbooli *et al.;* [16] Sachan *et al.;* [12] Morley *et al.;* [23] Gale *et al.;* [24] and Prentice *et al.;* [25] who also found no relation between vitamin D and neonatal anthropometry. However, Leffelaar *et al.;* [26] and Bowyer *et al.;* [27] found that vitamin D deficient mothers had lower birth weight in new-borns. The conflicting results can be explained as our study of vitamin D was in late pregnancy, rather than early pregnancy, when factors affecting fetal growth have the greatest impact, differences in population characteristics and race/ethnicity and maternal or fetal genotype. Morley *et al.;* [20] observed that infant vitamin D receptor (VDR) polymorphisms modified the effect of maternal 25(OH) D on offspring size.

Therefore, in view of research reporting mixed findings, longitudinal research is required to systematically examine the relationship between maternal vitamin D status and neonatal outcome. Since maternal vitamin D deficiency leads to rickets and postnatal growth failure, it needs a long term follow up study to find other effects of maternal vitamin D deficiency in their offspring.

LIMITATION

The limitation of our study was that only 25(OH) D level was measured which is one member of the vitamin D family. At birth, there are potential changes in levels of vitamin D binding protein, 1, 25(OH) 2D, the CYP27 enzyme and expression of vitamin D receptors, which may influence the fetal growth. Second, 25(OH) D levels at birth cannot represent the vitamin D status in early pregnancy. Third, dietary habits, outdoor activity, environmental factors and genetic variation may result in residual confounding in this study. Finally, this study was conducted in one city and caution is needed in generalizing the findings.

CONCLUSION

Vitamin D deficiency is widely prevalent in our population. This shows that current maternal Vitamin D supplementation during pregnancy is not enough to build up adequate new born Vitamin D stores. More research is needed before a nationwide policy for recommendations on proper dosage of vitamin D during pregnancy can be justified.

Cord blood S. Calcium, S. Phosphorus and S. ALP do not seem to be reliable functional markers of vitamin D deficiency in new born. The long term impact of vitamin D deficiency on fetal and childhood skeletal development and the most appropriate dose and duration for vitamin D supplementation remains an important area of study.

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