ORIGINAL ARTICLE

Effect of Antenatal Oral Vitamin D Supplementation on Serum 25(OH)D Concentration in Exclusively Breastfed Infants at 6 Months of age - A Randomized Double-Blind Placebo-Controlled Trial

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ABSTRACT

Objective: To compare the proportion of exclusively breastfed (EBF) infants having severe vitamin D deficiency (25(OH)D concentration <11 ng/mL) at 6 months of age when mothers were supplemented with 300,000 IU vitamin D3 or placebo during the third trimester of pregnancy.

Methods: In this randomized double-blind placebo-controlled trial, we recruited 100 pregnant women (who were willing to exclusively breastfeed their babies for 6 months) at 30-32 weeks gestation and the infants born to them. Pregnant women were randomized to receive either oral vitamin D3 60,000 IU or placebo, given weekly for 5 weeks during the third trimester. Serum 25(OH)D, calcium, phosphorus and alkaline phosphatase concentration were measured in all participants at recruitment, in the cord blood at delivery, and in infants at 6 months of age. The proportion of infants developing severe vitamin D deficiency and rickets at 6 months was assessed.

Results: A total 72 mother-infant dyads were followed-up till 6 months. At enrollment, the mean (SD) serum 25(OH)D concentration (ng/mL) were comparable in mothers in the intervention and control groups [12.9 (5.8) vs 12.8 (5.9), $P = 0.96$]. The mean (SD) 25(OH)D concentration (ng/mL) in the cord blood was significantly higher in the intervention group compared to the control group [42.1 (17.1) vs 12.7 (6.3); $P = 0.002$]. Serum 25(OH)D levels (ng/mL) in the infants at 6 months age were higher in the intervention group compared to the control group [31.8 (10.9) vs 12.5 (5.7); $P < 0.001$]. No infant in the intervention group had severe vitamin D deficiency at 6 months age compared to 54.3% infants in the control group ($P < 0.001$). No infant in the intervention group developed rickets.

Conclusion: Oral supplementation of vitamin D3 to pregnant women in the third trimester prevents severe hypovitaminosis D in the EBF infants at 6 months of age.

Keywords: *Breastfeeding, Infants, Pregnant, Rickets*

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INTRODUCTION

There is a high prevalence of vitamin D deficiency among pregnant and lactating mothers and their infants [1-4]. In the past few decades, there has been an increase in the incidence of vitamin D deficiency in women and children due to lifestyle and dietary changes [5,6]. Women who breastfeed are particularly at greater risk of developing vitamin D deficiency [6]. Studies continue to show a very high prevalence of vitamin D deficiency in infants (42%-74%), and pregnant (44%-66%) and lactating mothers (70%-80%) [2,7-9].

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There is evidence that maternal vitamin D deficiency during pregnancy increases the risk of pre-eclampsia, gestational diabetes, fetal growth restriction and poor neonatal health [1,9]. Prenatal vitamin D supplementation reduces the risk of small for gestational age (SGA) babies without any adverse effects [10]. Vitamin D deficiency in infants not only leads to rickets [11] but is also associated with long-term morbidities like type 1 diabetes, respiratory illnesses and neurological diseases [3,11].

Vitamin D stores in the newborn depend solely on the maternal vitamin D concentration during pregnancy [12]. Naik et al reported that 77.3% of women had hypovitaminosis D (serum 25-hydroxy vitamin D, 25(OH)D <20 ng/mL) at parturition and one third of them suffered from severe vitamin D deficiency [25(OH)D <11 ng/mL]. The cord blood 25(OH)D concentration suggested severe vitamin D deficiency and hypovitaminosis D in 67.2% and

96.4% of infants at birth respectively [13]. As pregnant mothers are vitamin D deficient themselves, their infants accrue low vitamin D stores in the womb [14] and this deficiency extends to the lactating period if corrective measures are not taken [3]. The low anti-rachitic activity in the breastmilk creates a perfect milieu leading to a vitamin D deficient state in the exclusively breastfed (EBF) child [15].

Vitamin D supplementation in pregnant women increases the 25(OH)D concentration in the cord blood [16,17] and breastmilk [15]. The present study was, therefore, designed to determine the effect of antenatal vitamin D supplementation during the third trimester on the vitamin D status of the EBF infants at birth and at 6 months of age and the proportion of infants developing rickets at 6 months of age.

METHODS

This study was a randomized double-blind placebo-controlled trial conducted in the Department of Pediatrics of a tertiary care teaching hospital in collaboration with the Departments of Obstetrics and Gynecology and Endocrinology. Prior approval was obtained from the Institutional Ethics Committee for Human Research.

Pregnant women aged 19-35 years, and residing within 10 km of the hospital, were approached during their regular visits to the antenatal clinic at 30-32 weeks of pregnancy. Women with spontaneous conception, height >145 cm, prepregnancy weight > 45 kg, hemoglobin concentration > 9g/dL (at the time of enrollment) and BP < 140/90 mmHg and urine dipstick test negative for proteins and who were willing to exclusively breastfeed their babies were considered eligible for inclusion and were enrolled after taking written informed consent. Relevant demographic detail and obstetric history were recorded.

Neonates delivered to these mothers were thoroughly examined in the labour room and gestational age was confirmed by Modified Ballard Scoring. Neonates born at term (37 to 41 completed weeks) and appropriate for gestational age with an APGAR score >7 at 1 minute with no gross congenital anomalies on clinical examination were included. Neonates who developed seizures, sepsis, birth asphyxia or required exchange transfusion or those who received vitamin D in infancy were excluded. Women suffering from chronic illnesses like tuberculosis, seizure disorder, diabetes mellitus, chronic liver, and kidney disease, hypothyroidism, hypoparathyroidism, and those who had received additional vitamin D within the last 3 months (apart from elemental calcium 500mg, vitamin D3 250 IU given twice daily in the antenatal clinic under the national program) were excluded.

Participants were randomized using a computer-generated randomization sequence, to receive either oral cholecalciferol or placebo (inert sugar) dispensed as capsule form. The drug and placebo were coded as A or B and serially numbered from 1-100 by a third person not associated with the study. The allocation of a mother-infant dyads to either group was done by serially numbered opaque sealed envelope (SNOSE) technique. On completion of the study, the decoding was done in two steps. First, the serial numbers were converted to either A or B and a master chart was prepared, and then data analysis was done. After results were available, further decoding revealed that pregnant mothers in group A received vitamin D and those in group B received a placebo.

Each capsule contained either 60,000IU of cholecalciferol or inert sugar (placebo) and were identical in appearance and smell. The capsules for both groups were specially prepared by Mankind Pharmaceuticals Ltd. for the study purpose. At recruitment 3 mL venous blood sample was drawn from each mother and the first dose of drug was administered under direct supervision of the research team. Subsequent doses were administered at weekly follow up visits under direct supervision. Thus, each mother either received 300,000 IU of cholecalciferol (5 capsules of 60,000 IU vitamin D3 each) or a placebo.

At birth, 3 mL cord blood was collected, and anthropometry of the newborn was recorded. Mothers were counselled to exclusively breastfeed their infants till 6 months of age. Exclusive breastfeeding is defined as no other food or drink, not even water, except breastmilk (including milk expressed or from a wet nurse) given to the infant till 6 months of life, but allowed the infant to receive oral rehydration solution (ORS), vitamins, minerals, and medicines in the form of drops or syrups [18].

Mothers were counselled to expose the infants' fixed surface area (face, forearms, and legs comprising 32% of total body surface area) under sunlight for 15 minutes/day between 10 AM and 3 PM and to note the number of days of sunlight exposure per week in a chart provided to them. Compliance to fill the chart was ensured telephonically on a weekly basis.

Each infant was followed up at 6 (+1) weeks, 10 (+1) weeks, 14 (+1) weeks and 6 months (+2 weeks) of age wherein anthropometry and duration of sunlight exposure was recorded. Sunlight exposure was estimated using Sun Index [19] which was calculated as:

Weekly sun index = Body surface area exposed to sunlight x Hours of exposure/week

Total sun index = Weekly sun index x Total weeks of exposure

Cord and venous blood samples collected at birth and at 6 months, respectively, were centrifuged and sera separated and stored at -20°C for estimation of 25(OH)D, calcium, phosphorus, and alkaline phosphatase (ALP) concentration. Estimation of serum 25(OH)D concentration was done by chemiluminescence immune assay (CLIA) (Access 2 Immunoassay Analyzer of Beckman Coulter Co.). Digital radiographs of both wrists (AP view) were obtained to detect radiological rickets in infants; presence of cupping, splaying, or fraying at the lower end of radius/ulna was regarded as radiographic evidence of rickets. Serum ALP > 420 IU/mL was considered as biochemical rickets. Vitamin D deficiency, insufficiency and sufficiency was defined as serum 25(OH)D levels < 11 ng/mL, < 20 ng/mL and ≥ 20 ng/mL, respectively [20].

We could not find any study wherein vitamin D supplementation was given to pregnant mothers in their third trimester and the prevalence of vitamin D deficiency in their breastfed infants was assessed at 6 months. Based on a study conducted in our institution by Naik et al [13], wherein lactating mothers were supplemented with 600,000 IU vitamin D3 or placebo in the early postpartum period, 7.5% of EBF infants in the supplemented group and 43.8% in the placebo group had vitamin D deficiency [25(OH) D level < 11 ng/mL]. So, to detect a difference of 50% change in the proportion of EBF infants having achieved 25(OH)D levels > 11ng/mL in the intervention group at 6 months of age, with type 1 error at 5% and power of study 80%, the required number of infants in each group was 35. A total of 70 pregnant mothers and their infants were required for the study. Based on our hospital data, we estimated that 30% of newborns would be excluded on account of being SGA, preterm, non-vigorous delivered through meconium-stained liquor, having birth asphyxia, seizures, congenital anomalies and requiring exchange transfusion. Considering 10% dropout during follow-up, 100 consecutive pregnant mothers fulfilling the inclusion criteria were recruited comprising 50 mother-baby dyads in each group.

Statistical analysis: The data was analyzed using SPSS version 20. Descriptive statistics representing mean and standard deviation (SD) or median and interquartile range (IQR) were determined for quantitative variables, and Qualitative variables were presented as numbers and percentages. Normality of data were examined using box whisker plot and Shapiro-Wilk test. Normally distributed variables were compared between the two groups using unpaired student's t-test while those not normally distributed were compared using Mann-Whitney U test. Correlation between 25(OH)D levels and other variables was reported as Spearman correlation coefficient. Chi square/ Fisher exact test was applied to compare the proportion of qualitative variables between the two groups.

RESULTS

Out of 100 pregnant mothers enrolled in the study, 72 mother-infant pairs (37 infants in the vitamin D supplementation group and 35 infants in the placebo group) were followed-up for 6 months. Maternal parameters were comparable in both the groups (**Table I**) with almost 90% pregnant mothers having vitamin D insufficiency and 25% with severe deficiency. The

Table I Baseline Demographic and Laboratory Characteristics of Pregnant Women

Maternal Parameters	*Vitamin D supplementation group (n = 37)*	*Placebo group (n = 35)*	*P value*
Anthropometry			
Weight (kg)	56.90 (7.16)	57.40 (8.96)	0.75
Height(cm)	151.26 (1.70)	151.00 (2.33)	0.52
BMI (kg/m^2)	24.85 (3.02)	25.14 (3.66)	0.66
Age (y)	24.30 (2.07)	24.80 (2.49)	0.27
Dietary habit [a]			
Lacto vegetarian	26 (52)	29 (58)	0.90
Lacto-ovo-vegetarian	4 (8)	4 (8)	
Non-vegetarian	20 (40)	17 (37)	
Dressing habit [a]			
Fully covered	5 (10)	6 (12)	0.74
Partially covered	45 (98.3)	44 (92.9)	
Educational status[a]			
Primary	10 (20)	11 (22)	0.71
Secondary	27 (54)	23 (46)	
Graduate	13 (26)	16 (32)	
Parity (P)[a]			
P0 (nulliparous)	32 (64)	25 (50)	0.21
P1	17 (34)	21 (42)	
P2 or more	1 (2)	4 (8)	
Serum calcium (mg/dL)	7.9 (2.2)	8.4 (2.0)	0.43
Serum phosphorus (mg/dL)	3.7 (1.5)	3.6 (1.2)	0.28
Serum alkaline phosphatase (IU/mL)	141.6 (79.5)	153.5 (83.0)	0.46
Serum 25(OH)D levels (ng/mL)	12.9 (5.8)	12.8 (5.9)	0.96
Serum 25(OH)D levels < 20 ng/mL[a]	33 (89.2)	32 (91.4)	1.00
Serum 25(OH)D levels < 11 ng/mL[a]	21 (56.8)	23 (65.7)	0.47

25(OH)D 25-hydroxy vitamin D, BMI Body mass index; Values expressed as mean (SD) or [a]n (%)

baseline and 6 months anthropometric parameters of infants were comparable in both the groups (**Table II**).

The mean cord blood 25(OH)D concentration was significantly higher in the intervention group which was maintained even at 6-months of age (**Table III**). The difference in the 25(OH)D concentration between the two groups was maintained even after adjustment for independent variables like – birth weight, maternal, cord blood vitamin D levels and total sunlight exposure affecting serum vitamin D levels. We also found a positive correlation between vitamin D levels in cord blood and at 6-months of age in both intervention arm (r = 0.34, *P* = 0.03) and the placebo arm (r = 0.56, *P* < 0.001]. At 6-months, biochemical profile was comparable in both groups except ALP (**Table III**). The mean (SD) Sun Index from birth to 14 weeks and from 14 weeks to 6 months was comparable in both groups [2.44 (0.96) vs 2.51 (1.00), *P* = 0.76; 1.73 (0.66) vs 1.77 (0.69), *P* = 0.70 respectively].

Three infants developed biochemical rickets and two infants suffered from radiological rickets in the placebo group compared to none in the intervention group. There was no clinical evidence of hypervitaminosis D in infants during follow-up and none required urinary calcium-creatinine ratio.

DISCUSSION

In this randomized controlled trial, 100 pregnant women were recruited and 60,000IU vitamin D3 or placebo was administered weekly for 5 weeks. Cord blood was collected after delivery and mothers were counselled for exclusive breastfeeding till 6 months of age. The possible confounders like maternal body mass index (BMI), baseline 25(OH)D levels, dietary habits, dressing preferences and Sun Index were comparable in both groups. Our study revealed a high prevalence of vitamin D deficiency among pregnant women as was observed in the previous studies from India [2] and abroad [1].

We found that infants born to mothers supplemented with vitamin D in the antenatal period had a significantly higher level of 25(OH)D in their cord blood and even at 6 months of age compared to the placebo group. None of the infants born to vitamin D supplemented mothers had severe vitamin D deficiency at 6 months. This was possible only when sufficient vitamin D was transferred to the

Table II Growth Profile of Neonates at Birth and at 6 Months of age

	Vitamin D supplementation group (n = 37)	*Placebo group (n = 35)*	*P value*
Growth parameters at birth			
Gestation (wk)	38.6 (1.2)	38.4 (1.2)	0.49
Birth weight (g)	2920 (280)	2810 (290)	0.88
Length (cm)	51.5 (2.4)	50.5 (1.8)	0.35
Head circumference (cm)	33.9 (1.3)	33.7 (1.2)	0.41
Chest circumference (cm)	31.4 (1.5)	31.2 (1.6)	0.93
Anterior fontanelle (cm^2)	5.1 (2.0)	5.7 (2.3)	0.27
Growth parameters at 6 months of age			
Weight (g)	7490 (630)	7630 (650)	0.15
Length (cm)	65.8 (2.0)	65.3 (2.4)	0.71
Head circumference (cm)	43.6 (1.6)	43.5 (1.6)	0.89
Chest circumference (cm)	44.0 (2.9)	44.3 (2.1)	0.17
Anterior fontanelle (cm^2)	1.0 (1.5)	2.3 (3.9)	0.16

Values expressed as mean (SD)

Table III Biochemical Profile of Neonates at Birth and at 6 Months of age

	Vitamin D group (n = 37)	*Placebo group (n = 35)*	*P value*
At birth (cord blood)			
Serum calcium (mg/dL)	8.4 (1.3)	7.6 (1.2)	0.01
Serum phosphorus (mg/dL)	4.3 (1.1)	4.2 (1.3)	0.70
Serum alkaline phosphatase (IU/mL)	79.5 (44.3)	99.7 (20.4)	0.01
Serum 25(OH)D (ng/mL)	42.1 (17.1)	12.7 (6.3)	0.002
Proportion with serum 25 (OH)D < 20 ng/mL[a]	0	31 (88.6)	< 0.001
Proportion with serum 25 (OH)D < 11 ng/mL[a]	0	22 (62.9)	< 0.001
At 6 months of age			
Serum 25(OH)D (ng/mL)	31.8 (10.9)	12.5 (5.7)	< 0.001
Serum calcium (mg/dL)	9.3 (2.1)	8.6 (1.9)	0.79
Serum phosphorus (mg/dL)	5.2 (0.8)	5.6 (1.2)	0.22
Serum alkaline phosphatase (IU/mL)	161.0 (83.2)	241.8 (122.3)	0.02
Proportion with 25(OH)D < 20 ng/mL[a]	2 (5.4)	31 (88.6)	0.002
Proportion with 25(OH)D < 11 ng/mL[a]	0 (0)	19 (54.3)	< 0.001
Proportion with hypo-calcemia[a]	8 (21.6)	15 (42.8)	0.05
Proportion with hypo-phosphatemia[a]	5 (13.5)	8 (22.8)	0.30
Proportion with radio-logical/biochemical rickets[a]	0 (0)	5 (14.2)	0.01

Values expressed as mean (SD) or [a]n (%). 25(OH)D 25-hydroxy vitamin D

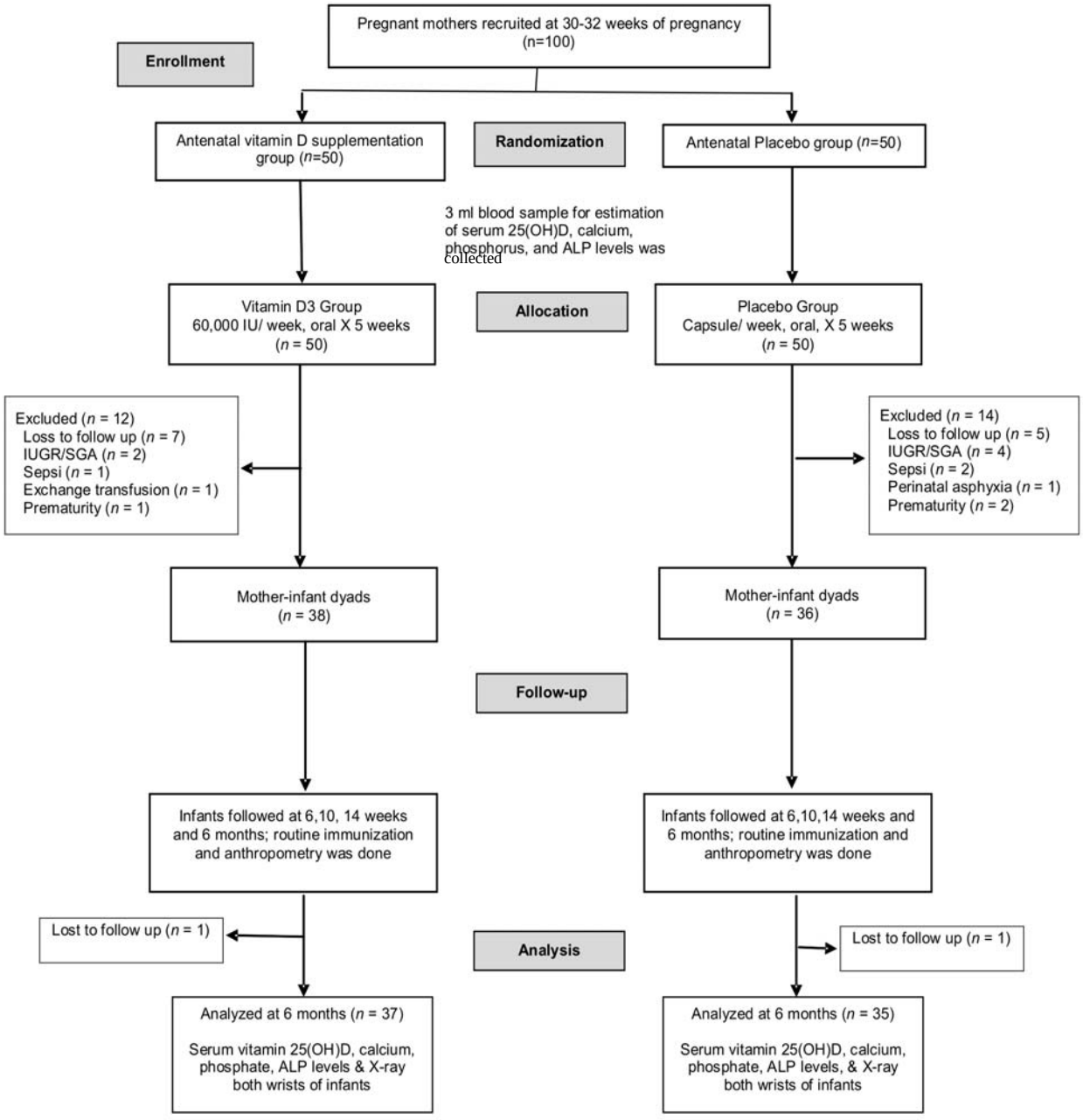

Fig.1 Consort Flow Diagram of Study Participants

developing fetus throughout pregnancy. Antenatal vitamin D supplementation must also have increased the 25(OH)D levels of the mothers and subsequently in the breast milk, although we did not measure it. Increased amount of vitamin D passed to the infants through breastfeeding in the vitamin D supplemented mothers, which further augmented levels of 25(OH)D in the infants. Hollis et al in a study found that mean 25(OH)D in maternal serum and cord blood at the time of delivery was greatest in pregnant women supplemented with 4000IU cholecalciferol daily from 12-16 weeks of pregnancy till delivery [17]. Roth et al conducted a double-blind randomized trial in which mothers were supplemented with either placebo or 35000 IU/week vitamin D3 during third trimester till delivery and the level of 25(OH)D was found to be significantly higher in the cord blood of vitamin D supplemented group [16]. A recent systemic review has shown a significantly higher cord blood 25(OH)D levels in mothers supplemented with vitamin D during pregnancy compared to unsupplemented mothers [21,22].

There is a strong positive correlation between 25(OH)D levels in maternal serum, cord blood [13,23] and breastmilk [23]. We also found a significantly higher level of vitamin D in cord blood of infants in supplemented arm. As cord blood concentration represents neonatal vitamin D stores, these findings suggest that, antenatal supplementation of vitamin D results in higher newborn stores which subsequently prevents vitamin D deficiency in EBF infants even at 6 months of age.

Several recent studies have demonstrated that maternal 25(OH)D levels correlate directly with infants' 25(OH)D values, implying that maternal vitamin D intake directly affects the vitamin D status of their infants [24]. Maximum fetal calcium demand occurs during the third trimester, and optimal vitamin D levels are crucial during this period for both maternal health and fetal outcome [24].

A study assessing the effect of high dose vitamin D supplementation (2800 IU/day) during pregnancy has shown an improved bone mineralisation and less incidence of fracture at 6 years of age in the offspring compared to those supplemented with standard dose (400 IU/day), and no change in anthropometric parameters [25]. We also found no difference in the anthropometric parameters between the two groups, but infants in the placebo group developed rickets (biochemical and radiological) while those in the intervention group were protected at 6 months of age.

Our study's limitation is that sample size was based on maternal supplementation of vitamin D during breastfeeding and not during pregnancy. Another limitation is that we did not measure 25(OH)D levels in the mothers at the time of delivery and at 6 months postpartum due to financial constraints. The strength of our study is the double-blind randomized placebo-controlled design of the study and adequate follow up. Moreover, we used highly sensitive CLIA technique to measure 25(OH)D.

None of the infants born to mothers who received 300,000 IU of vitamin D in the antenatal period had 25(OH)D levels < 11ng/mL at 6 months of age as against 54.3% (n = 19) of infants in the placebo group. Thus, antenatal supplementation prevented severe vitamin D deficiency in infants at 6 months of age. This can have long-term implications like decreased incidence of respiratory, metabolic and neurological illness in these children later in life. Maternal supplementation can be a new prudent approach which will not only prevent vitamin D deficiency in infants but will also correct deficiency in mothers. Although a history of high dose vitamin D intake must be taken to prevent hypervitaminosis. Further multicentric studies with large sample size are required to strengthen the findings of our study to incorporate it as a recommendation.

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REFERENCES

1. Kiely ME, Wagner CL, Roth DE. Vitamin D in pregnancy: Where we are and where we should go. J Steroid Biochem Mol Biol. 2020;201:105669.
2. Sharma N, Nath C, Mohammad J. Vitamin D status in pregnant women visiting a tertiary care center of North Eastern India. J Family Med Prim Care. 2019;8:356-60.
3. Mansur JL, Oliveri B, Giacoia E, Fusaro D, Costanzo PR. Vitamin D: Before, during and after pregnancy: Effect on neonates and children. Nutrients. 2022;14:1900.
4. Agarwal N, Faridi MMA, Aggarwal A, Singh O. Vitamin D status of term exclusively breastfed infants and their mothers from India. Acta Paediatr. 2010;99:1671-4.
5. Palacios C, Gonzalez L. Is vitamin D deficiency a major global public health problem? J Steroid Biochem Mol Biol. 2014;144:138-45.
6. Gellert S, Ströhle A, Hahn A. Breastfeeding woman are at higher risk of vitamin D deficiency than non-breastfeeding women - Insights from the German Vita Min Femin study. Int Breastfeed J. 2016;12:19.
7. Trivedi M, Faridi MMA, Aggarwal A, Madhu SV, Malhotra RK. Oral Vitamin D supplementation to mothers during lactation-effect of 25(OH)D concentration on exclusively breastfed infants at 6 months of age: A randomized double-blind placebo-controlled trial. Breastfeed Med. 2020;15: 237-45.
8. Kamboj P, Dwivedi S, Toteja GS. Prevalence of hypovitaminosis D in India & way forward. Indian J Med Res. 2018;148:548-56.
9. Bi WG, Nuyt AM, Weiler H, Leduc L, Santamaria C, Wei SQ. Association between vitamin D supplementation during pregnancy and offspring growth, morbidity, and mortality:

A systematic review and meta-analysis. JAMA Pediatr. 2018;172:635-45.
10. Moon RJ, Green HD, D'Angelo S, et al. The effect of pregnancy vitamin D supplementation on offspring bone mineral density in childhood: A systematic review and meta-analysis. Osteoporosis Int. 2023;34:1269-79.
11. Pérez-López FR, Pilz S, Chedraui P. Vitamin D supplementation during pregnancy: An overview. Curr Opin Obstet Gynecol. 2020;32:316-21.
12. Marwaha RK, Tandon N, Chopra S, et al. Vitamin D status in pregnant Indian women across trimesters and different seasons and its correlation with neonatal serum 25-hydroxyvitamin D levels. Br J Nutr. 2011;106:1383-9.
13. Naik P, Faridi MMA, Batra P, Madhu S V. Oral supplementation of parturient mothers with Vitamin D and its effect on 25OHD status of exclusively breastfed infants at 6 months of age: A double-blind randomized placebo controlled trial. Breastfeed Med. 2017;12:621-8.
14. Kaushal M, Magon N. Vitamin D in pregnancy: A metabolic outlook. Indian J Endocrinol Metab. 2013;17:76-82.
15. Dawodu A, Tsang RC. Maternal vitamin D status: Effect on milk vitamin D content and vitamin D status of breastfeeding infants. Adv Nutr. 2012;3:353-61.
16. Roth DE, Al Mahmud A, Raqib R, et al. Randomized placebo-controlled trial of high-dose prenatal third-trimester vitamin D3 supplementation in Bangladesh: The AViDD trial. Nutr J. 2013;12:47.
17. Hollis BW, Johnson D, Hulsey TC, Ebeling M, Wagner CL. Vitamin D supplementation during pregnancy: Double-blind, randomized clinical trial of safety and effectiveness. J Bone Miner Res. 2011;26:2341-57.
18. World Health Organization. Indicators for assessing infant and young child feeding practices. Part I definition. Geneva. World Health Organization, 2008.
19. Meena P, Dabas A, Shah D, et al. Sunlight exposure and vitamin D status in breastfed infants. Indian Pediatr. 2017;54:105-11.
20. Rosen CJ, Abrams SA, Aloia JF, et al. IOM Committee Members respond to Endocrine Society Vitamin D Guideline. J Clin Endocrinol Metab. 2012;97:1146-52.
21. Luo T, Lin Y, Lu J, et al. Effects of vitamin D supplementation during pregnancy on bone health and offspring growth: A systematic review and meta-analysis of randomized controlled trials. PLoS One. 2022;17: e0276016.
22. Wong RS, Tung KTS, Mak RTW, et al. Vitamin D concentrations during pregnancy and in cord blood: A systematic review and meta-analysis. Nutr Rev. 2022;80: 2225-36.
23. Wagner CL, Hollis BW. Early-life effects of vitamin D: A focus on pregnancy and lactation. Ann Nutr Metab. 2020;76:16-28.
24. Abrams SA. In utero physiology: Role in nutrient delivery and fetal development for calcium, phosphorus, and vitamin D. Am J Clin Nutr. 2007;85:604S-7S.
25. Brustad N, Garland J, Thorsen J, et al. Effect of high-dose vs standard-dose vitamin D supplementation in pregnancy on bone mineralization in offspring until age 6 years: A prespecified secondary analysis of a double-blinded, randomized clinical trial. JAMA Pediatr. 2020;174:419-27.