RESEARCH PAPER

Effect of Maternal Supplementation With Two Different Doses of Vitamin D During Lactation on Vitamin D Status, Anthropometry and Bone Mass of Infants: *A Randomized Controlled Trial*

Rekha Ramot,[1] Swati Yadav,[2] SK Vishnoi,[2] Pramod Sharma,[2] Rajesh Khadgawat,[1] Rakesh Jora[2]

From [1]Department of Endocrinology and Metabolism, All India Institute of Medical Sciences, New Delhi; [2]Department of Pediatrics, Dr S N Medical College, Jodhpur, Rajasthan.

Correspondence to: Prof Rakesh Jora, Department of Pediatrics, Dr SN Medical College, Jodhpur, Rajasthan. jorarakesh@gmail.com

Received: March 10, 2021; Initial review: June 09, 2021; Accepted: December 18, 2021.

Background: There is a high prevalence of vitamin D deficiency (VDD) in exclusively breast-fed infants in the absence of appropriate vitamin D supplementation.

Objective: To evaluate the efficacy of two doses of maternal vitamin D supplementation on vitamin D levels of mother-infant pairs and to assess its effect on growth parameters (weight, length and head circumference) and bone mass of infants.

Study design: Randomized controlled trial.

Participants: Lactating mother-infant pairs (*n*=220).

Intervention: Maternal oral vitamin D supplementation in two doses (group 1: 1,20,000 IU/month and group 2: 12,000 IU/month) for 12 months.

Main outcomes: Maternal and infant serum 25OHD levels, and infants' growth and bone mass.

Results: There was high prevalence of VDD at baseline in mothers (94%) as well as infants (98.5%), which was reduced to 43.1% in (mothers) and 46.5% in infants after 12 months. Significantly higher median (IQR) serum 25OHD levels (ng/mL) were observed among mothers in group 1 compared to group 2 [46 (17-159) vs 18 (6-64); *P*<0.01] and in infants [36.5 (15-160) vs 17 (7-32); *P*<0.01]. No significant association was observed between growth parameters or bone mass and serum 25OHD levels of mother or infant between the two groups. Four mothers (3.6%) and two infants (1.8%) in group I had serum 25OHD>100 ng/mL, but without hypercalciuria or hypercalcemia.

Conclusion: Bolus vitamin D supplementation in the dose of 1,20,000 IU/month was more efficacious in improving maternal and infant vitamin D status at 12 months, as compared to 12,000 IU/month.

Keywords: *Bone densitometry, DXA, Lactating mothers, Vitamin D deficiency.*

Published online: January 09, 2022; ***PII:*** S097475591600396

Vitamin D deficiency (VDD) in infancy and childhood is a serious public health concern in Asia, Middle East, and North Africa [1]. A high prevalence of VDD is reported among infants, depending on the definition and the latitude of the population studied [2]. The prevalence of VDD among nursing mothers and their breast-fed infants has been widely reported from India [3,4].

Breast milk is a poor source of vitamin D (~5-80 IU/L) [5], which predisposes exclusively breast-fed infants to an increased risk of developing rickets as compared to vitamin D fortified formula-fed infants [6]. A strong positive correlation has been reported between vitamin D intake of lactating mothers and serum 25-hydroxy vitamin D (25OHD) levels of infants. A sufficient maternal vitamin D intake is associated with optimal vitamin D transfer via breast milk which is adequate to meet infant needs [7]. The Indian Academy of Pediatrics recommends oral supplementation of 400 IU/day of vitamin D to all breastfed infants up to one year of age [8]. However, the practical applicability of this recommendation is questionable as adherence was found to be less than <20% [9]. Therefore, high-dose vitamin D supplementation to lactating mothers seems to be a better approach to address the dual problem of VDD in lactating mother-infant pairs [5].

Invited Commentary: Pages 274-75

Indian data on optimal dose of vitamin D supplementation among lactating mothers to improve vitamin D status of infants is scarce. Therefore, the present study was planned with the primary objective to evaluate the efficacy of two vitamin D supplementation doses (1,20,000 IU/month vs 12,000 IU/month) to lactating mothers on serum 25OHD levels of mother-infant pairs. The effect of maternal vitamin D supplementation on infant's anthropometry and whole body bone mass were also studied as secondary objectives.

METHODS

The present randomized controlled trial was conducted from December, 2014 to December, 2017 after ethical approval. The subjects were enrolled after written informed consent.

Healthy breast-fed mother-infant pairs within one month of delivery, willing to follow-up for 12 months were included. Mothers with pre-existing type 2 diabetes, hypertension, chronic renal or liver disease, antipsychotic drug exposure, clinical osteomalacia or severe vitamin D deficiency or exposure to medications known to affect vitamin D metabolism were excluded. Infants with congenital malformations and birth asphyxia were excluded. Additionally, mothers with serum calcium >11mg/dL, serum 25OHD level >100 ng/mL, liver enzymes elevated >3 times upper limit of normal (ULN) and serum creatinine above ULN for age at screening were also excluded.

The mothers were randomized (using computer-generated simple random code) into two groups (1:1 ratio) of oral vitamin D supplementation: 1,20,000 IU/month (group 1) and 12,000 IU/month (group 2) for 12 months. The vitamin D dose 400 IU/day (group 2) was chosen considering high prevalence VDD in India and ICMR-NIN recommendation [10], while the dose of 4000 IU/day (group I) was chosen based on recommendations of the Endocrine Society to maintain serum 25OHD ≥30ng/mL in exclusively breast-fed infants not on vitamin D supplements [11]. The vitamin D supplements were administered as telephonically supervised monthly bolus doses for better compliance. All the subjects were advised to regularly go-out in sun on a daily basis (the city where study was conducted has abundant sunshine throughout the year). Vitamin D preparations were provided as oral tablets (strength 12,000 IU and 1,20,000 IU); unlabelled for dose and identical in all aspects of colour, taste, and external appearance (Torrent Pharmaceuticals).

The safety of intervention was assessed by measurement of corrected total serum calcium and urinary calcium: creatinine ratio (non-fasting, second void sample) at baseline, six months, and 12 months. Hypercalcemia was defined as a total serum calcium level of >11 mg/dL and hypercalciuria as urinary (spot urine sample) calcium: creatinine ratio >0.4 [12]. Subjects with urinary calcium: creatinine ratio of >0.4 without hypercalcemia were re-evaluated with a timed 24-hour urine calcium excretion and 4 mg/kg excretion was considered as abnormal. Any subject, who developed both hypercalcemia and hypercalciuria was excluded from further intervention.

The biochemical parameters (complete blood counts, liver and renal function tests, total serum calcium, phosphate, total alkaline phosphatase, and blood glucose) were measured using Roche Hitachi 912 Chemistry Analyzer (GMI, Inc.), serum 25OHD was assessed using chemiluminescent assay using LIASON (DiaSorin Inc.) auto analyzer. The reproducibility of the assay ranged from 6% to 12%, and the laboratory was registered with UK-DEQAS vitamin D assay external quality control assessment program (*www.deqas.org*). The vitamin D status was categorized as: severe deficiency, deficiency, insufficiency, and sufficiency based on serum 25OHD levels (ng/mL) of <10, <20, 20-29, and ≥30, respectively [13].

The whole body bone mass of infant was assessed by dual-energy *X*-ray absorptiometry (DXA) using GE Lunar Prodigy Advance instrument 8743 (GE Medical systems) at 12 months (±15 days). The scans were conducted with uniform swaddling of infants in fed and sleeping state without sedation. In order to obtain artefact-free scans, appropriate positioning of infants was achieved by securing the infant's upper extremities away from the trunk region and gently binding of both the upper and lower extremities using a cotton blanket. The scans with movement artefacts were excluded.

The birthweight of infants was measured to the nearest 10 g using an electronic weighing scale, length to nearest 0.5 cm using an infant measuring board, and head circumference to the nearest 0.1 cm using a non-stretchable tape.

The sample size was calculated based on the presumption that 10% subjects in the control arm and 40% subjects in the intervention group would achieve maternal serum 25OHD >30 ng/mL after one year. Hundred subjects in each arm were required to detect the above difference with 90% power and 97.5% confidence levels. Anticipating 20% dropouts, 110 subjects were required to be enrolled in each arm.

Statistical analysis: This was carried out using STATA14.2 (StataCorp LLC). The appropriately coded data were entered in Microsoft Excel from case record forms, and extreme values (beyond 1.5 times of inter-quartile range below Q1 or above Q3) were excluded. Continuous variables were compared by independent *t*-test (normally distributed) or Wilcoxson rank sum test (non-normally distributed) and within group comparison was assessed using paired *t*-test (normally distributed). The linear regression was applied to assess the association between maternal and infant vitamin D status as well as the association of infant vitamin D status with bone mass.

RESULTS

A total of 220 mother-infant pairs (138 multiparaous

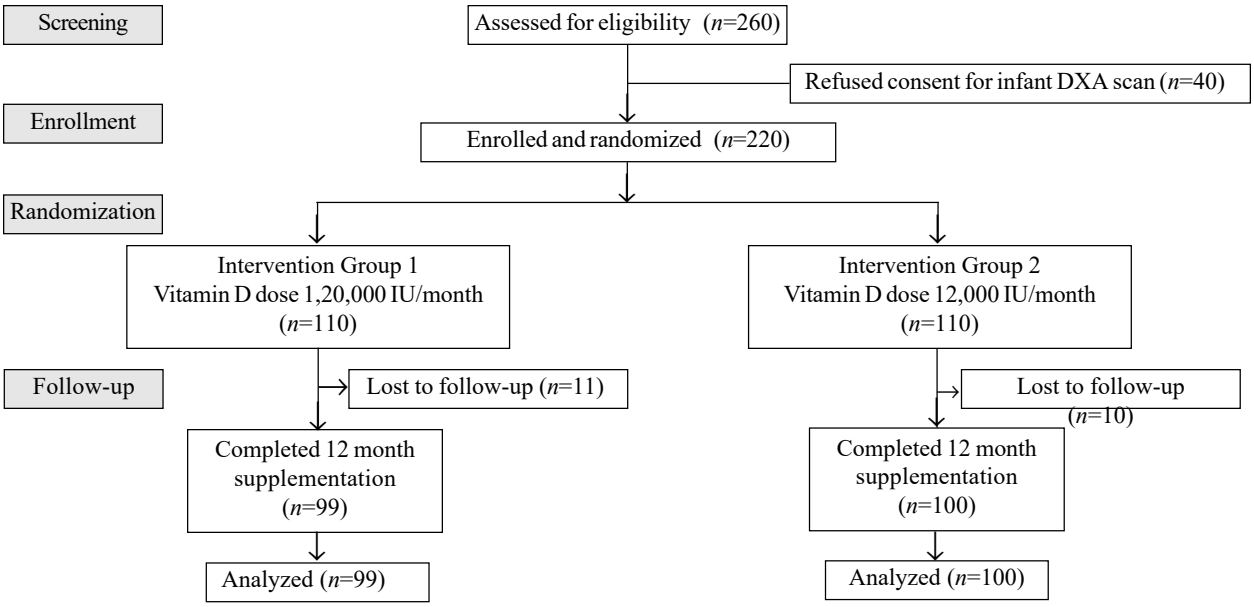


Fig. 1 Flow chart of study participants.

Table I Baseline Maternal and Infant Characteristics

Variable	*Group 1*	*Group 2*
Maternal characteristics	(*n*=110)	(*n*=110)
Age, y	25.3 (4.6)	24.8 (4.3)
Height, cm	156.05 (6.4)	157.6 (5.7)
BMI, kg/m^2	23.07 (3.9)	23.6 (4.3)
Gestational age, wk	38.6 (1.01)	38.2(1.3)
Infant characteristics		
Normal birthweight	*(n=90)*	*(n=95)*
Weight, kg	2.8 (0.4)	2.9 (0.4)
Length, cm	48.4 (1.66)	48.4 (1.96)
Head circumference, cm	33.3 (1.10)	33.1 (1.18)
Low birthweight	*(n=20)*	*(n=15)*
Weight, kg	2.3 (0.13)	2.20 (0.19)
Length, cm	46.9 (2.7)	44.5 (1.8)
Head circumference, cm	32.1 (1.38)	32 (1.26)

Data expressed as mean (*SD*). *BMI: body mass index.*

mothers; 114 male infants) were randomized into two groups (**Fig. 1**). Baseline demographic characteristics of the study population are presented in **Table I**.

The median (range) of maternal and infant serum 25OHD levels of entire group at baseline were 8.3 (0.4-30.1) and 5.8 (0.2-33.8) ng/mL, respectively, which was not significantly different between the two groups (**Table II** and **III**). There was a high prevalence of VDD in mothers (94%) and infants (98.5%) at baseline (**Web Table I**).

Maternal serum 25OHD levels of ≥30 ng/mL and >20-30 ng/mL were seen in 73 (73.7%) and 18 (18.2%) in group 1, and 5 (5%) and 17 (17%) in group 2 at 12 months. Among infants, 75 (75.7%) and 19 (19.2) had serum 25OHD ≥30 and >20-30 mg/mL in group 1, while in group 2, only 5 and 13 infants had ≥30 and >20-29 ng/mL serum 25OHD levels, respetively. The proportion of infants with serum 25OHD <20 ng/mL reduced to 5 (5%) in group I but increased to 82 (82%) in group 2 (**Web Table I**). The comparison of vitamin D status of mothers and infants with respect to supplementation groups is presented in **Fig. 2**.

Increased (mean) urinary calcium:creatinine ratio (>0.4) was observed in 3 (0.63), 5 (0.73), and 1 (0.88) mother at baseline, six months, and 12 months, respectively. However, none of these subjects developed hypercalcemia (symptomatic or asymptomatic) and hypercalciuria, or both. Only two infants had serum 25OHD levels >100ng/mL after 12 months of supplementation (both belonged to group 1); however, none of them developed hypercalciuria or hypercalcemia.

There was no significant difference in anthropometric growth parameters (length, weight and head circumference) of infants between the two groups at baseline as well as at one year (P>0.05) (**Table IV**).

The vitamin D status of mother and infant was significantly correlated at baseline as well as at 12 months. With each ng/mL increase in maternal serum 25OHD, infant serum 25OHD increased by 0.55 ng/mL (95% CI 0.36 to 0.74) after 12 months of supplementation.

Table II Maternal Biochemical Parameters at Baseline and 12 Months in the Two Groups

Parameter	*Group I*			*Group II*		
	Baseline (n=110)	*Follow-up (n=99)*	*Mean diff (95% CI)*	*Baseline (n=110)*	*Follow up (n=100)*	*Mean diff (95% CI)*
Calcium; mg/dL	9.2 (0.88)	8.7 (0.87)	-0.46 (-0.71, -0.21)[b]	9 (0.92)	8.8 (0.87)	-0.25 (-0.51, 0.02)
Phosphate; mg/dL	4.8 (0.59)	4.5 (0.87)	-0.35 (-0.56, -0.14)[b]	5.01(0.62)	4.5 (0.85)	-0.46 (-0.66, 0.26)[b]
ALP, IU/L	214.9 (69.95)	170.6 (39)	-44.3 (-58.6, -29.9)[b]	226.6 (78.54)	163.6 (36.48)	-62.3 (-79.9, 44.6)[b]
25OHD, ng/mL[a]	9.2 (6.3, 12.5)	46 (29, 69)	44.9 (39.4, 50.4)[b]	7.8 (4.1,12.2)	18 (16, 20)	9.9 (8.1, 11.8)[b]
Albumin, g/dL	2.9 (0.36)	3.6 (0.74)	0.69 (0.52, 0.85)[b]	2.9 (0.38)	3.5 (0.74)	0.66 (0.51, 0.81)[b]
Urinary calcium/ creatinine[a]	0.07 (0.04, 0.13)	0.09 (0.04, 0.16)	-	0.07 (0.03,0.15)	0.07 (0.04, 0.14)	-

Data represented as mean (SD) or [a]median (IQR). Maternal vitamin D supplementation Group I- 120000 IU/mth and Group II- 12000 IU/mth. [b]P<0.05. ALP-alkaline phosphatase; 25OHD-25-hydroxy vitamin D.

Table III Infant Biochemical Parameters at Baseline and 12 Months in the Two Groups

Serum levels	*Group I*			*Group II*		
	Baseline (n=110)	*Follow-up (n=99)*	*Mean diff (95% CI)*	*Baseline (n=110)*	*Follow up (n=100)*	*Mean diff (95% CI)*
Calcium, mg/dL	9.2 (1.0)	8.8 (0.89)	-0.48 (-0.74, -0.21)[b]	9.3 (0.9)	8.8 (0.88)	-0.43 (-0.66, 0.19)[b]
Phosphate, mg/dL	4.9 (0.85)	4.9 (0.84)	0.006 (-0.23, 0.24)	5.01 (0.73)	5.09 (0.80)	0.07 (-0.16, 0.31)
ALP, IU/L	259.2 (113.09)	280 (112.2)	20.9 (-9.16, 50.9)	252.1 (108.53)	296 (105.85)	43.9 (15.9,71.9)
Albumin, g/dL	3.03 (0.49)	3.6 (0.67)	0.56 (0.39, 0.73)[b]	3.1 (0.45)	3.6 (0.80)	0.47 (0.28, 0.66)[b]
25OHD, ng/mL[a]	7.1 (4.3, 9.2)	36.5 (30.5, 56)	36.9 (32.7, 41.2)[b]	4.8 (2.7 to 9.2)	17 (14.2,19)	12.05 (10.6, 14.4)[b]

Data represented as mean (SD) or [a]median (IQR). Maternal vitamin D supplementation Group I-120000 IU/mth and Group II-12000 IU/mth. [b]P<0.05. ALP: alkaline phosphatase; 25OHD: 25-hydroxy vitamin D.

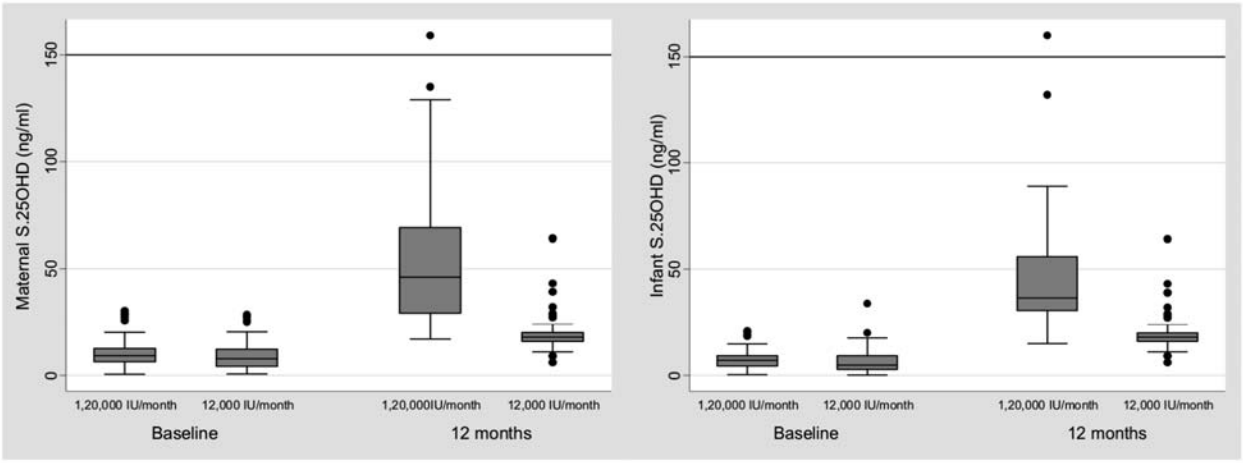
There was no significant difference in infant bone mass parameters between the two groups after one year of supplementation (**Table IV**). The mean BMC, BMD, and bone area of LBW infants were significantly lower as compared to the corresponding values of normal birth weight infants ($P<0.05$). The infant bone mass was not significantly associated with maternal age, BMI, and maternal serum 25OHD parameters (baseline, at 12 months and delta-change) in both the groups. Similarly, the infant's vitamin D level at baseline, at 12 months, and delta-change in serum 25OHD levels were also not significantly associated with bone mass parameters (**Web Table II**).

The infant's weight at birth as well as 12 months was significantly associated with bone mass parameters in both the groups (all $P<0.05$). Each 100 g increase in birth weight was associated with a mean (95% CI) increase in BMC, BMD and bone area by 0.004 (0.001 to 0.004) g, 0.26 (0.79 to 4.61) g/cm^2 and 0.0002 (0.0016 to 0.002) cm^2, respectively for group 1, and for group 2, 0.005 (0.001 to 0.006) g, 0.28 (0.35 to 5.17) g/cm^2 and 0.0002 (0.0005 to 0.003) cm^2, respectively. Similar increases were also observed irrespective of the groups without any significant difference between the groups.

DISCUSSION

The present study assessed the effects of vitamin D supplementation of two doses (1,20,000) IU/month vs 12,000 IU/month) for 12 months on serum 25O HD levels of lactating mothers and infants, and reports a significant improvement in vitamin D status of both mothers and infants. The serum 25O HD levels of mothers and infants randomized to higher dose were significantly higher as compared to the lower dose group.

In comparison to the global data, a higher prevalence of VDD has been reported across all age groups in the Indian population [3,4,14,15]. Exclusively breastfed infants



a *b*

Fig. 2 Vitamin D status in the two treatment groups (*a*) mothers and (*b*) infants.

are at higher risk of developing VDD as breastmilk has insufficient vitamin D content (10 to 20% of maternal blood vitamin D levels) [16]. This is further compromised by a high prevalence of VDD in the mother. Daily maternal vitamin D supplementation of 4000-6400 IU/day to mothers is recommended to maintain serum 25OHD concentration >30 ng/mL in exclusively breastfed infants not on vitamin D supplements [7,17]. The cholecalciferol readily passes to breast milk by simple diffusion across the cell membranes into the milk while 25OHD requires the presence of vitamin D binding proteins (megalin-cubilin endocytotic system) [18]. It has been suggested that for every 1000 IU per day cholecalciferol intake by mother, milk antirachitic activity would increase by <80 IU/L [19].

Table IV Comparison of Anthropometry and Bone Mass of Infants in the Two Groups

Parameter	*Group 1*	*Group 2*	*P value*
Anthropometry			
Normal birthweight	*n=90*	*n=95*	
Weight, kg	8.5 (0.98)	8.4 (0.97)	0.47
Length, cm	74 (3.19)	74 (2.80)	0.98
Head circumference, cm	44.2 (1.51)	44.1 (1.41)	0.78
Low birthweight	*n=20*	*n=15*	
Weight, kg	8.1 (0.9)	7.8 (0.9)	0.38
Length, cm	72.8 (3.61)	72.9 (2.72)	0.92
Head circumference, cm	43.4 (1.22)	43.9 (1.24)	0.29
Bone mass parameters			
Normal birthweight	*n=90*	*n=95*	
BMC, g	126.3 (29.67)	123.2 (23.65)	0.42
BMD, g/cm^2	0.323 (0.04)	0.320 (0.03)	0.57
Area, cm^2	387.6 (53.46)	383.5 (47.58)	0.56
Low birthweight	*n=20*	*n=15*	
BMC, g	110.2 (27.09)	*106.4 (19.73)*	0.65
BMD, g/cm^2	0.297 (0.04)	0.297 (0.03)	0.97
Area, cm^2	366.8 (49.9)	*355.3 (34.77)*	0.45

Data expressed as mean (SD).

The MAVID randomized controlled trial compared vitamin D supplementation of 1200 IU/day to mothers with 400 IU/day given to babies and reported a similar increase in serum 25OHD level of infants in both groups. However, mothers in the first group had significantly higher serum 25OHD levels [20]. Similarly, another study, using a higher dose of cholecalciferol supplementation (6400 vs 300 IU/day to mothers for six months) showed significantly higher serum 25OHD levels in mothers and breast milk, but not in infants [19]. Similar results have also been reported in other studies [17,21,22]. Our study also reported similar results, with a significant increase in serum 25OHD levels of mothers as well as infants in both the groups. These differences with earlier studies (VDD in <30% subjects) could be because of a large difference in baseline vitamin D status.

Supplementation of vitamin D in daily dose is more physiological; however, the bolus dose (weekly or monthly) is equally effective in terms of improving vitamin D status with a higher adherence rate [23]. Comparison of daily vs bolus dose of vitamin D supplementation in lactating mothers showed equal efficacy [24]. We used bolus doses of vitamin D for supplementation, which gave us a very high compliance rate with minimal dropouts (<5% in both groups). Maintaining a high compliance rate for the study population, which is not highly educated (~60% of the study population was educated up to middle school

WHAT IS ALREADY KNOWN?

- Maternal vitamin D supplementation improves maternal and infant vitamin D status, and may be given in higher doses than those currently recommended.

WHAT THIS STUDY ADDS?

- Maternal vitamin D supplementation with a dose of 1,20,000 IU per month is more efficacious and safe than 12,000 IU per month in Indian population.

only, data not presented), is a significant advantage for countries with limited health resources.

There is limited evidence on whether maternal vitamin D supplementation during lactation improves infant growth. No effect on infant's weight, length, and head circumference was reported earlier even after controlling for confounding factors, similar to the present study. However, the majority of subjects did not have VDD [21]. Studies from regions where VDD is common have also shown similar results [25]. The present study also had a high proportion of maternal VDD but did not show any significant difference in infant's anthropometry.

The effects of maternal vitamin D supplementation on infant bone mass parameters have not been clearly evaluated. The MAVID trial reported no significant differences in infant whole-body BMC or BMD between the intervention (1200 IU/day) vs the control group (400 IU/day) of maternal vitamin D supplementation for six months [20]. Likewise, greater than 90% of the study subjects in the present study had VDD at baseline, but significant difference was not seen in whole body bone mass parameters between the two groups.

Due to logistic issues, we could not carry out estimation of vitamin D content in breast milk, which would have given an insight regarding the appropriate dose of maternal vitamin D supplementation. The details of supplementary feeding, which might have contributed to additional vitamin D intake by the infant, were not captured. Similarly, the details of sun exposure by mothers-infants and seasonal variability were not captured. However, we presume these variables would have affected both the groups similarly as subjects were randomized. It would have been better if infants were supplemented directly (like 400 IU/day) and compared with supplementation of lactating mother in improving vitamin D status of infant. However, in view of poor compliance of direct vitamin D supplementation in infant [9], this was not planned. The estimation of serum PTH was not planned due to logistic reasons (storage and transportation).

In conclusion, the present study shows that bolus vitamin D supplementation of lactating mothers (starting from the first postpartum month) in the dose of 1,20,000 IU/month was more efficacious to improve maternal and infant vitamin D status in comparison to 12,000 IU/month. However, vitamin D supplementation did not affect growth and bone mass parameters of infants.

Ethics clearance: Ethics Committee, Dr SN Medical College; No. F.1/Acad/MC/JU/13/ 16276, dated August 21, 2013.
Contributors: RK, RJ: contributed in conceptualising, planning and design of the study, data collection, analysis and interpretation of results and writing of manuscript; RR: involved in data collection, analysis and manuscript writing; SKV,PS,SW: involved in data collection. All authors approved the final version of manuscript, and are accountable for all aspects related to the study.
Funding: Department of Health Research (DHR), Ministry of Health and Family Welfare, Government of India (Grant No-GIA/68/2014-DHR).
Competing interests: None stated.
Note: Additional material related to this study is available with the online version at *www.indianpediatrics.net*

REFERENCES

1. Thacher TD, Fischer PR, Strand MA, Pettifor JM. Nutritional rickets around the world: causes and future directions. Ann Trop Paediatr. 2006;26:1-16.
2. Rovner AJ, O'Brien KO. Hypovitaminosis D among healthy children in the United States: A review of the current evidence. Arch Pediatr Adolesc Med. 2008;162: 513-19.
3. Bhalala U, Desai M, Parekh P, et al. Subclinical hypovitaminosis D among exclusively breastfed young infants. Indian Pediatr. 2007;44:897-901.
4. Seth A, Marwaha RK, Singla B, et al. Vitamin D nutritional status of exclusively breast fed infants and their mothers. J Pediatr Endocrinol Metab. 2009;22:241-6.
5. Food and Nutrition Board. Standing Committee on the scientific evaluation of dietary reference intakes. Dietary Reference Intakes for Vitamin D and Calcium. National Academy Press; 2010.
6. Widdowson EM. Food intake and growth in the newly-born. Proc Nutr Soc. 1971;30:127-35.
7. Thiele DK, Senti JL, Anderson CM. Maternal vitamin D supplementation to meet the needs of the breastfed infant: A systematic review. J Hum Lact. 2013;29:163-70.
8. Khadilkar A, Khadilkar V, Chinnappa J, et al. Prevention and Treatment of Vitamin D and Calcium Deficiency in Children and Adolescents: Indian Academy of Pediatrics

(IAP) Guidelines. Indian Pediatr. 2017;54:567-73.
9. Perrine CG, Sharma AJ, Jefferds ME, et al. Adherence to vitamin D recommendations among US infants. Pediatrics. 2010; 125:627-32.
10. Indian Council of Medical Research. Nutrient Requirements and Recommended Dietary Allowances for Indians 2010. Accessed December 02, 2021. Available from: *https://www.icmr.nic.in/content/nutrient-requirements-recommended-dietary-allowances-indians*
11. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, Treatment, and Prevention of Vitamin D Deficiency: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2011;96:1911-3.
12. Vieth R, Chan PC, MacFarlane GD. Efficacy and safety of vitamin D3 intake exceeding the lowest observed adverse effect level. Am J Clin Nut. 2001;73:288-94.
13. Holick MF. Vitamin D deficiency. N Engl J Med. 2007; 357:266-81.
14. Khadgawat R, Marwaha RK, Garg MK, et al. Impact of vitamin D fortified milk supplementation on vitamin D status of healthy school children aged 10-14 years. Osteoporos Int. 2013;24:2335-43.
15. Jain V, Gupta N, Kalaivani M, et al. Vitamin D deficiency in healthy breastfed term infants at 3 months and their mothers in India: Seasonal variation and determinants. Indian J Med Res. 2011;133:267-73.
16. Hollis BW, Frank NE. Quantitation of vitamin D2, vitamin D3, 25-hydroxyvitamin D2, and 25-hydroxyvitamin D3 in human milk. Methods Enzymol. 1986;123:167-76.
17. Hollis BW, Wagner CL, Howard CR, et al. Maternal versus infant vitamin D supplementation during lactation: A randomized controlled trial. Pediatrics. 2015;136:625-34.
18. Hollis BW, Wagner CL. The role of the parent compound vitamin D with respect to metabolism and function: Why clinical dose intervals can affect clinical outcomes. J Clin Endocrinol Metab. 2013;98:4619-28.
19. Wagner CL, Hulsey TC, Fanning D, et al. High-dose vitamin D3 supplementation in a cohort of breastfeeding mothers and their infants: A 6-month follow-up pilot study. Breastfeed Med. 2006;1:59-70.
20. Czech-Kowalska J, Latka-Grot J, Bulsiewicz D, et al. Impact of vitamin D supplementation during lactation on vitamin D status and body composition of mother-infant pairs: A MAVID randomized controlled trial. PLoS One. 2014; 9:e107708.
21. Hollis BW, Wagner CL. Vitamin D requirements during lactation: High-dose maternal supplementation as therapy to prevent hypovitaminosis D for both the mother and the nursing infant. Am J Clin Nutr. 2004;80:1752S-58S.
22. Dawodu A, Salameh KM, Al-Janahi NS. The effect of high-dose postpartum maternal vitamin D supplementation alone compared with maternal plus infant vitamin D supplementation in breastfeeding infants in a high-risk population: A randomized controlled trial. Nutrients. 2019;11:1632.
23. Meekins ME, Oberhelman SS, Lee BR, et al. Pharmacokinetics of daily versus monthly vitamin D3 supplementation in non-lactating women. Eur J Clin Nutr. 2014; 68:632-34.
24. Oberhelman SS, Meekins ME, Fischer PR, et al. Maternal vitamin D supplementation to improve the vitamin D status of breast-fed infants: A randomized controlled trial. Mayo Clin Proc. 2013;88:1378-87.
25. Roth DE, Morris SK, Zlotkin S, et al. Vitamin D supplementation in pregnancy and lactation and infant growth. N Engl J Med. 2018; 379:535-46.

CLIPPINGS

C3 Glomerulopathy and related disorders in children - Etiology-phenotype correlation and outcomes (Clin J Am Soc Nephrol. 2021;16:1639-51)

Membranoproliferative glomerulonephritis (MPGN) is a histopathological entity characterized by increased mesangial matrix and cellularity along with thickening of glomerular capillary walls, resulting from dysregulation of the alternative complement pathway. It is broadly classified into C3 glomerulopathy [C3 glomerulonephritis (C3GN) and Dense deposit disease (DDD)] and immune complex MPGN. This multicenter observational cohort study enrolled 80 pediatric (2-15 years) patients with MPGN/C3 glomerulopathy to determine the phenotype and were followed up for a median of 5.18 (IQR, 2.13-8.08) years within the National Registry of Rare Kidney Diseases (RaDaR). C3GN was more common than immune complex MPGN (39 vs 31 patients) while 10 patients were identified with immune complex GN. Acquired (anticomplement autoantibodies) alternate pathway dysregulation was detected in 46% patients across all groups while genetic alterations contributed to only 9% of patients. Hematuria was the most common presentation (91%) and low estimated glomerular filtration rate (eGFR) was detected in 44% patients at recruitment. Importantly, severe kidney dysfunction (eGFR <30 mL/min per 1.73 m^2) was observed only in patients with C3GN. On follow up, complete or partial remission was observed in 28 patients (71%) with C3GN and 36 patients (88%) with immune complex MPGN. Eleven patients (14%) progressed to renal failure and histopathologic evidence of >50% crescents was found to be the only risk factor for renal failure in multivariate analysis (hazard ratio, 6.2; 95% confidence interval, 1.05 to 36.6; $P<0.05$). Nine transplants were performed in eight patients but 2 of these failed due to recurrent disease. The authors concluded that presenting eGFR and crescentic disease are important prognostic markers of C3GN in pediatric patients, and even though acquired complement pathway abnormalities are common among these patients, they do not contribute to renal failure.

DR PRAJAL AGARWAL
prajal.agarwal@gmail.com