

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

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

PII: S097475591600396

Note: This early-online version of the article is an unedited manuscript that has been accepted for publication. It has been posted to the website for making it available to readers, ahead of its publication in print. This version will undergo copy-editing, typesetting, and proofreading, before final publication; and the text may undergo minor changes in the final version.

ABSTRACT

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: 120 000 IU/month and group 2: 12000 IU/month for 12 months).

Main-outcomes: Maternal and infant serum 25OHD levels, and infant's 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.*

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 (25O HD) 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 400IU/day of vitamin D to all breast-fed 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].

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 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 1) was chosen based on recommendations of the Endocrine Society to maintain serum 25OHD ≥ 30 ng/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., Stillwater, 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 - 29 , and ≥ 30 , respectively [13].

The whole-body bone mass of infant was assessed by 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 birth-weight of infants was measured to the nearest 10g using an electronic weighing scale, length to nearest 0.5cm 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, 120 subjects were required to be enrolled in each arm.

Statistical analysis: This was carried out using STATA14.2 (StataCorp LIC). 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 Wilcoxon 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 multi-paraous mothers; 114 male infants) were randomized into two groups (**Fig. 1**). Baseline demographic characteristics of the study population are presented in **Table I**, which showed no significant difference.

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, 5 (5%) and 17 (17%) in group 2 at 12 months. Among infants, 75 (75.7%), and in 19 (19.2) had serum 25OHD ≥ 30 and >20 - 30 mg/mL group 1, while in group 2, only 5 and 13 infants had ≥ 30 and >20 - 29 ng/mL serum 25OHD levels. 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. 2a** and **b**.

Increased (mean) urinary calcium:creatinine ratio (>0.4) was observed in three (0.63), five (0.73), and one (0.88) mothers 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 $>100\text{ng/mL}$ 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 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.

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, the 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 . 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 25OHD levels of lactating mothers and infants and reports a significant improvement in vitamin D status of both mothers and infants. The serum 25OHD 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 breast-fed infants are at higher risk of developing VDD as breast milk 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 $>30\text{ ng/mL}$ in exclusively breast-fed 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].

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 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, >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's 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. CTRI could not be registered prospectively.

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.

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.

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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; 25-OHD – 25-hydroxy vitamin D.

Table II Maternal Biochemical Parameters at Baseline and 12 Months

Parameter	Group I ^{#b}			Group II ^{#b}		
	Baseline (n=110)	Follow-up (n=99)	Mean diff (95% CI) ^c	Baseline (n=110)	Follow up (n=100)	Mean diff (95% CI) ^c
S Calcium; mg/dL	9.2(0.88)	8.7(0.87)	-0.46 (-0.71 to -0.21) ^c	9(0.92)	8.8 (0.87)	-0.25 (-0.51to0.02)
S Phosphate; mg/dL	4.8(0.59)	4.5(0.87)	-0.35 (-0.56 to -0.14) ^c	5.01(0.62)	4.5 (0.85)	-0.46 (-0.66 to 0.26) ^c
S ALP, IU/L	214.9(69.95)	170.6(39)	-44.3 (-58.6 to -29.9) ^c	226.6(78.54)	163.6(36.48)	-62.3 (-79.9 to 44.6) ^c
S 25OHD; ng/mL ^a	9.2(6.3 to 12.5)	46(29 to 69)	44.9 (39.4 to50.4) ^c	7.8 (4.1 to 12.2)	18 (16 to 20)	9.9 (8.1 to11.8) ^c
S Albumin; g/dL	2.9(0.36)	3.6(0.74)	0.69 (0.52 to0.85) ^c	2.9(0.38)	3.5 (0.74)	0.66 (0.51 to0.81) ^c
Urinary calcium/creatinine ^a	0.07 (0.04 to0.13)	0.09 (0.04 to0.16)	-	0.07 (0.03 to0.15)	0.07 (0.04 to0.14)	-

Data represented as mean (SD) or ^aMedian (Interquartile Range)

^b Represents dose of maternal vitamin D supplementation Group I- 120000IU/month and Group II- 12000IU/month;

^c significant mean difference (P<0.05); ALP – alkaline phosphatase; 25OHD – 25 – hydroxyl vitamin D

Table III Infant Biochemical Parameters at Baseline and 12 Months

Serum levels	Group I ^{#b}			Group II ^{#b}		
	Baseline (n=110)	Follow-up (n=99)	Mean diff (95% CI)	Baseline (n=110)	Follow up (n=100)	Mean diff (95% CI)
S Calcium, mg/dL	9.2(1)	8.8(0.89)	-0.48 (-0.74 to -0.21) ^c	9.3(0.9)	8.8(0.88)	-0.43 (-0.66 to 0.19) ^c
S Phosphate, mg/dL	4.9(0.85)	4.9(0.84)	0.006 (-0.23 to 0.24)	5.01(0.73)	5.09(0.80)	0.07 (-0.16 to 0.31)
S ALP, IU/L	259.2(113.09)	280(112.2)	20.9 (-9.16 to 50.9)	252.1(108.53)	296(105.85)	43.9 (15.9 to 71.9)
S Albumin, g/dL	3.03(0.49)	3.6(0.67)	0.56 (0.39 to 0.73) ^c	3.1(0.45)	3.6(0.80)	0.47 (0.28 to 0.66) ^c
S 25OHD ng/mL ^a	7.1(4.3to9.2)	36.5(30.5to56)	36.9 (32.7 to 41.2) ^c	4.8 (2.7to9.2)	17(14.2to19)	12.05 (10.6 to 14.4) ^c

Data represented as mean (SD) or ^a Median (Interquartile Range); ^b Represents dose of maternal vitamin D supplementation; Group I- 120000IU/month and Group II- 12000IU/month; ^c Indicates significant mean difference (P<0.05); ALP – alkaline phosphatase; 25OHD – 25 – hydroxyl vitamin D

Table IV Comparison of Anthropometry & Bone Mass of Infants

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 birth weight	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); P<0.05 for intragroup comparison between normal birth weight and low birthweight infants. BMC – bone mineral content, BMD – bone mineral density.

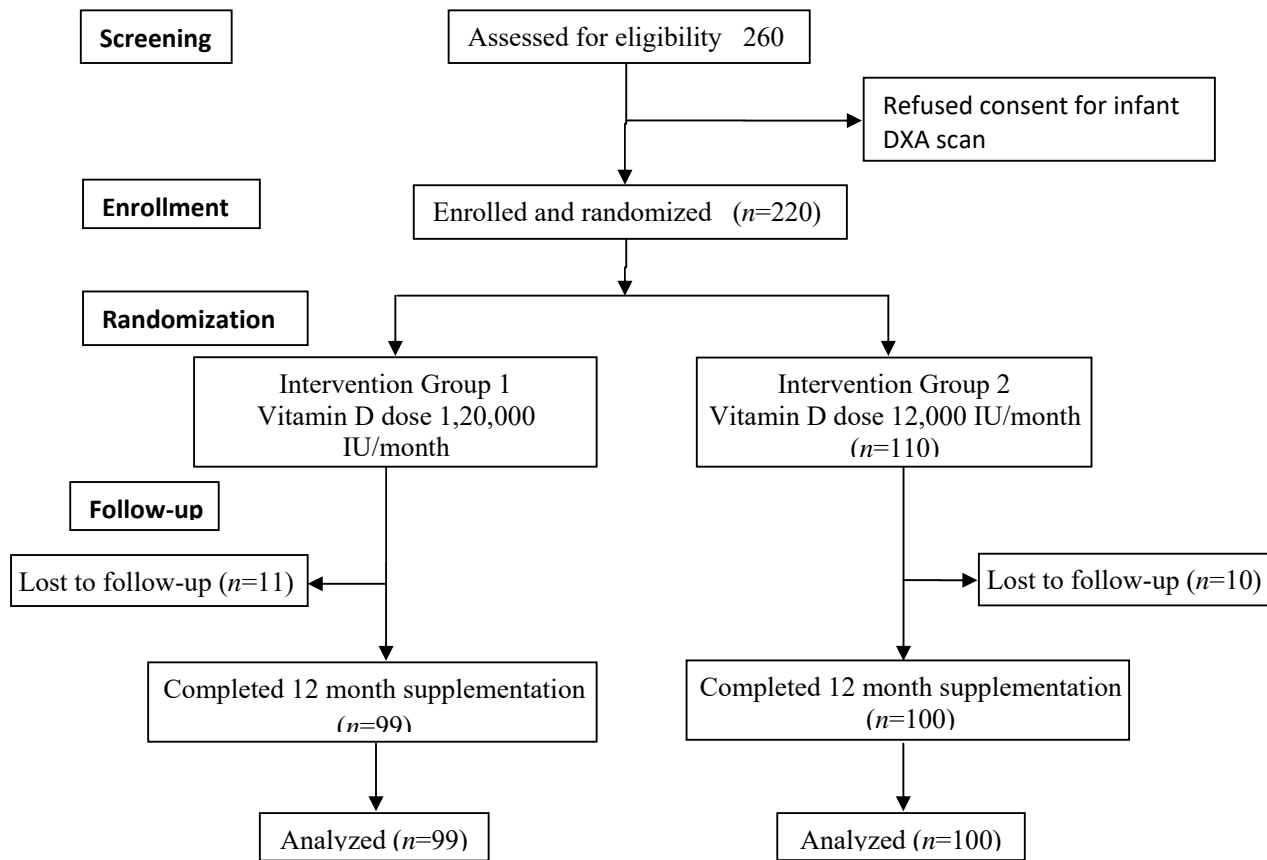


Fig. 1 Flow-chart of study participants

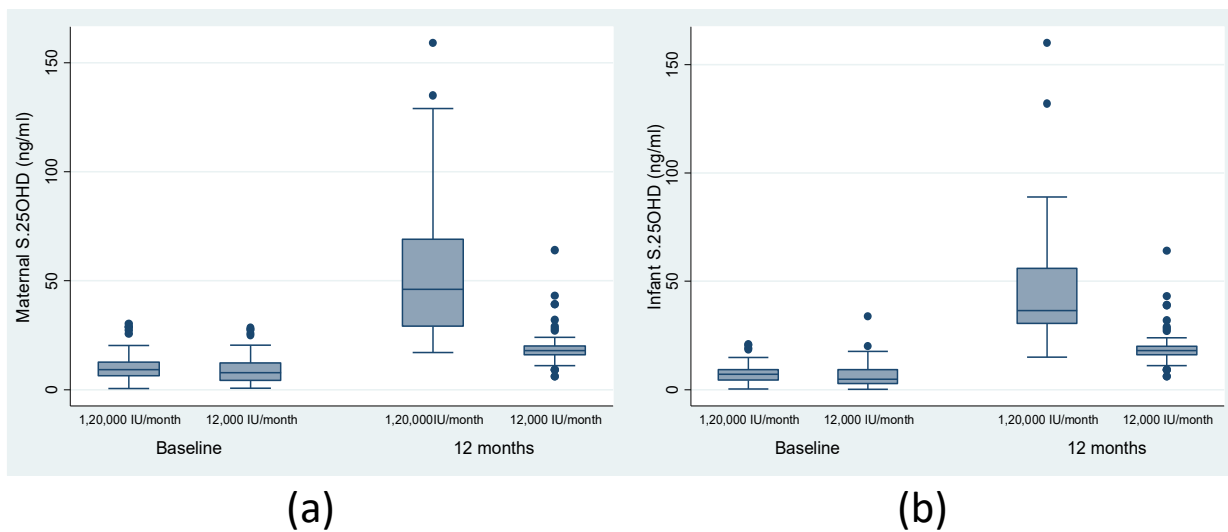


Fig 2. Vitamin D status Two Treatment Groups – (a) mothers; (b) infants.

Web Table I Vitamin D Status of Mother and Infants

Serum 25OHD, ng/mL	Group 1 [#] n(%)		Group 2 [#] n(%)	
	Baseline (n=110)	Follow-up (n=99)	Baseline (n=110)	Follow-up (n=99)
<i>Mother</i>				
<10	58(58.6)	-	63(63)	5(5)
10-20	35(35.3)	8(8.1)	31(31)	73(73)
21-30	5(5.05)	18(18.2)	6(6)	17(17)
≥30	1(1.01)	73(73.7)	-	5(5)
<i>Infant</i>				
<10	78(78.7)	-	78(78)	5(5)
10-20	19(19.2)	5(5.05)	21(21)	77(77)
21-30	2 (2.02)	19(19.2)	1(1)	13(13)
≥30	-	75(75.7)	-	5(5)

[#]Represents dose of maternal vitamin D supplementation ;Group I- 120000IU/month and Group II- 12000IU/month 25OHD – 25 – hydroxyl vitamin D

Web Table II Variation in Bone Mass Based on Maternal and Infant Vitamin D Status

Serum 25OHD, ng/mL	BMC (g)			BMD (g/cm ²)			Area (cm ²)		
	Group 1	Group 2	P Value	Group 1	Group 2	P Value	Group 1	Group 2	P Value
<i>Maternal baseline^a</i>									
<10	123.5(28.27)	121.6(22.6)	0.68	0.320(0.04)	0.317(0.03)	0.71	383(54.54)	381.5(44.39)	0.86
10-20	131.7(32.6)	126.6(27.45)	0.47	0.329(0.05)	0.325(0.03)	0.68	395.7(53.61)	385.9(57.12)	0.47
21-29	121.5(26.14)	125.4(11.08)	0.75	0.317(0.04)	0.319(0.01)	0.91	381.2(47.40)	392.2(25.26)	0.63
<i>Maternal 1 year</i>									
<10	-	103.7(17.45)	-	-	0.292(0.03)	-	-	352.7(32.98)	-
10-20	110.9(22.13)	124.5(22.53)	0.11	0.322(0.06)	0.319(0.03)	0.81	346(46.84)	388(43.06)	0.05
21-29	126.3(19.91)	126.8(28.62)	0.95	0.322(0.03)	0.330(0.04)	0.50	391.4(36.62)	382.7(58.11)	0.59
≥30	128(32.16)	112.2(20.10)	0.28	0.323(0.04)	0.321(0.01)	0.91	391.2(56.32)	351.4(72.13)	0.14
<i>Infant baseline^a</i>									
<10	126.4(29.88)	122.3(22.45)	0.33	0.325(0.04)	0.319(0.03)	0.37	385.9(55.33)	381.9(45.67)	0.62
10-20	126.8(31.65)	126(30.44)	0.94	0.319(0.04)	0.322(0.04)	0.83	392.5(51.33)	386.8(59.4)	0.76
21-29	#	#	-	#	#	-	#	#	-
<i>Infant 1 year^b</i>									
10-20	126.6(30.1)	123.1(24.53)	0.39	0.323(0.04)	0.320(0.03)	0.56	387.9(54.25)	382.7(49.35)	0.50
21-29	126.5(30.25)	126.1(17.74)	0.96	0.322(0.04)	0.320(0.03)	0.91	388.9(53.05)	393.3(40.06)	0.77
≥30	127.3(29.94)	#	-	0.322(0.04)	#	-	390.9(52.67)	#	-

Data expressed as Mean(SD); # Represents single observation, so Mean(SD) could not be calculated. ^aNone had value >30ng/mL.

^bNone had value <10ng/mL