

Hypocalcemia Due to Vitamin D Deficiency in Exclusively Breastfed Infants

S. Balasubramanian, So. Shivbalan, P. Saravana Kumar

From the Kanchi Kamakoti Childs Trust Hospital (KKCTH), 12- A, Nageswara Road, Nungambakkam, Chennai 600 034. Tamil Nadu, India.

Correspondence to Dr. S. Balasubramanian, Senior Consultant, Kanchi Kamakoti Childs Trust Hospital (KKCTH) 12-A, Nageswara Road, Nungambakkam, Chennai 600 034, India.

E-mail: sbsped53@sify.com

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This report is based on observations during the conduct of a study of hypocalcemia in infants and children. In a study of 50 cases, 13 exclusively breast fed infants manifesting with hypocalcemic seizures were confirmed to have vitamin D deficiency. None of the 13 infants had received vitamin D supplementation. All of them had biochemical evidence of hyperparathyroidism and low levels of 25 (OH) Vit D3 and promptly responded to therapy with vitamin D and calcium. All the mothers of these 13 infants had low levels of 25 (OH) Vit D3. Mothers of 5 infants had reported reduced exposure to sunlight due to religious reasons. This report emphasizes the need to supplement Vitamin D in exclusively breast fed infants and also to encourage exposure to sunlight in them and their mothers.

Keywords: *Exclusive breastfeeding, Hypocalcemia, Vitamin D deficiency.*

HYPOCALCEMIA is one of the common metabolic causes of seizures in children. The risk of hypocalcemia in exclusively breast-fed infants is less than that of artificially fed infants. Improper artificial feeds and lack of breastfeeding are common causes of hypocalcemia in infancy. Increasing trends in the incidence of hypocalcemia and vitamin D deficiency in infants and children without radiological evidence of rickets has been reported in UK recently(1). We encountered 13 exclusively breastfed infants less than 6 months of age, presenting with hypocalcemic seizures in whom vitamin D deficiency could be identified.

Subjects and methods

Thirteen exclusively breastfed infants were diagnosed to have hypocalcemic seizures due to vitamin D deficiency as a part of a study in which we were investigating all infants and

children presenting with hypocalcemic seizures (total of 50 cases) during the period from January 2002 to January 2004. Hypocalcemia was defined as serum calcium <8 mg/dL and ionized calcium <1 meq/L. In all these infants the following investigations were routinely carried out – complete blood counts, serum levels of calcium, ionized calcium, phosphate, alkaline phosphatase, albumin, magnesium creatinine, electrolytes, blood urea and sugar, skiagram of chest and both knees for evidence of rickets and Ultrasonogram of abdomen. Serum levels of vitamin D (25 OH-D3) and intact parathormone (iPTH) were estimated in all these infants. The iPTH was assayed by solid phase, two site Chem-luminescence method using Immulite analyser 2000 and the kit used was from Diagnostic Products Corporation, Los Angeles (PIL2KPP-13). 25OH vitamin D3 was assayed by I¹²⁵ radioimmunoassay by

Gamma Counter, using the kit from DiaSorin, Minnesota, USA (Ref. 681003). Vitamin D deficiency was diagnosed if serum 25OH vitamin D3 level was <10 ng/mL(2). Serum levels of calcium, phosphorus, alkaline phosphatase and Vitamin D (25 OH-D3) were estimated in the mothers of all these infants.

Results

The mean age of these infants was 3.8 months, the youngest being 2 months and the oldest being 6 months. Of these, 8 were males and 5 were females. The nutritional status of all these infants was uniformly normal with weight for length being $>90\%$ of the expected (as per Waterlow Classification). All were born at term and none of them had received vitamin D supplements. Rachitic rosary and craniotables were observed in one infant. Signs of rickets were not evident in the remaining 12 infants. Anthropometric evidence of catch up growth was not observed in any of them.

Biochemical investigations revealed that all these infants had hypocalcemia (decreased total and ionic calcium). Levels of blood sugar and serum levels of proteins, albumin, magnesium, urea, creatinine and electrolytes were normal in all the infants. But the levels of alkaline phosphatase were markedly elevated (Mean = 1250 IU/L) in all of them. Hypophosphatemia (<3.8 mg/dL) was observed in 9 out of these 13 infants (Table I). Serum vitamin D (25 OH vitamin D3) levels were low (Mean 3.8 ng/mL) and serum parathormone levels were elevated (Mean 106 pg/mL) in all these exclusively breastfed infants. Only 2 infants had radiological features of Rickets with findings of fraying of ends of long bones in the knees. Dilated cardiomyopathy as a complication was observed in 2 infants which responded to therapy with calcium and vitamin D. One of the thirteen infants had associated myelofibrosis(3) and died.

Vitamin D deficiency in all the mothers of these infants was biochemically proven (low 25 OHD3 levels) and none of the mothers had exhibited any overt clinical abnormality. All of them belonged to upper socio-economic status as per Modified Kuppusamy's classification. On enquiring about sunlight exposure to the mothers and infants, 5 out of the 13 mothers had stated that they had strictly followed the practice of covering their head and limbs completely while moving out of their houses (3 were Muslims and 2 were Jains).

All these infants were treated with a single dose of vitamin D parenterally (Inj. Arachitol 6 lakhs IM). Calcium gluconate (10 %) was administered intravenously initially with a bolus dose of 2 mL/kg followed by 1 mL/kg every 6 hours until serum calcium and ionized calcium levels were >8 mg/dL and >1.0 mEq/L respectively. Normal calcium levels were achieved within a mean period of 3 days. Following this, oral calcium supplements (50 mg/kg/day) (calcium carbonate tablets) were administered for 2 months in all of them. Normal phosphate levels were restored over a mean period of 24 days (range 2 weeks to 2 months) whereas alkaline phosphatase reached normal levels for the age over a mean period of 2 months (range 25 days to 3 months).

On follow-up of 12 infants for six months, none had recurrence of seizures or hypocalcemia and all were clinically normal. All the mothers were also advised to have exposure to sunlight every day for themselves and their infants as well, in addition to supplementation of a multivitamin preparation with vitamin D (400 IU /day) for their infants. Thus a diagnosis of vitamin D deficiency was confirmed in these infants by the presence of biochemical evidence of low levels of 25 OHD3, hyperparathyroidism and prompt

TABLE I—Anthropometric Data and Biochemical Changes in 13 Infants with Vitamin D Deficiency.

S. No.	Age in months	Sex	* Weight for length (%)	Calcium mg/dL	Ionised Calcium mEq/L	Phosphorus mg/dL	Alkaline Phosphatase IU/L	PTH pg/mL	25 OH vitamin D ng/mL
Normal Range				8.8-10.8	1.0-1.3	3.8-6.5	145-420	9-65	7.4-53.3
1	3	M	95.4	7.2	0.81	3.2	987	82	5.0
2	4	F	94	6.8	0.73	3.4	1421	102	2.3
3	3.5	M	96	6.2	0.82	3.8	1120	128	4.0
4	4	F	97.3	7.4	0.73	4.1	1223	114	1.5
5	6	M	95	7.9	0.9	2.9	2697	180	5.0
6	2	M	94.3	7.2	0.92	3.5	1032	95	2.2
7	3½	F	97	5.6	0.62	3.8	834	110	8.0
8	4½	M	96.6	6.2	0.56	2.1	1030	85	7.2
9	5	M	97	7.5	0.86	3.2	692	93	4.5
10	3	F	94.2	6.0	0.5	2.7	1096	98	3.0
11	3	M	98.2	6.6	0.7	3.5	2042	107	2.1
12	4	M	96.1	5.7	0.8	3.7	1172	92	1.5
13	4	F	93.9	7.0	0.95	4.5	904	94	4.0
Mean ± S.D.				6.71 ±0.72	0.76 ±0.13	3.4 ±0.62	1250.4 ±545.09	106.15 ±25.44	3.86 ±2.07

• Waterlow classification; • Value <10ng/ml was the cutoff value for the diagnosis of Vitamin D Deficiency(2)

therapeutic response to vitamin D and calcium therapy.

Discussion

Exclusive breastfeeding is recommended upto 6 months with all its beneficial effects on child survival. However reports of biochemical evidence of vitamin D deficiency in breastfed infants both in developing and developed countries have been periodically appearing in medical literature. In a study conducted in Pakistan(4) high prevalence of vitamin D deficiency in breastfed infants and nursing mothers was observed wherein out of 65 cases studied, 55% of infants and 45% of nursing mothers (predominantly belonging to upper socio-economic status) were found to have low levels of vitamin D (25 OH D3). In

our series all the cases belonged to upper socio-economic status.

Recommendations for vitamin D supplements have been made to all dark skinned, breastfed infants based on the observations that more African American women breast feed, fewer infants receive vitamin D supplements and also that mothers and infants were less exposed to sunlight(5). Ethnic difference is believed to be due to the decreased penetration of ultraviolet rays with increased skin pigment resulting in lower maternal vitamin D levels. Other factors that play a role include cultural beliefs as in Muslim religion where women wear concealing clothing and minimize sunlight exposure to themselves and their children. In

Key Message

- Vitamin D deficiency is observed in exclusively breastfed infants and can present with hypocalcemic seizures.

our series of 13 cases, mothers of 5 infants had practised the custom of covering their heads and limbs while moving out of their homes due to cultural and religious beliefs and this could have contributed to vitamin D deficiency in them and their offspring. It has been reported in an earlier study from USA(6) that infant serum 25-OHD concentrations are significantly related to ultraviolet exposure and maternal serum 25-OHD concentrations. In the same study, exposure to sunshine for 30 minutes per week wearing only a diaper or 2 hours a week fully clothed without a hat had been estimated to maintain serum 25-OHD concentration above the lower limit of the normal range.

In a study of 29 cases of hypocalcemia, from New Delhi(7), vitamin D deficiency in exclusively breastfed infants was not observed and reported whereas in our study, 13 exclusively breast fed infants with hypocalcemic seizures and their mothers were proven to have vitamin D deficiency. Symptomatic hypocalcemia in young infants due to vitamin D deficiency has been reported in two studies from UK(1,8). In such cases hypocalcemia could be attributed to the increased metabolic demands of rapid growth, resulting in development of symptomatic hypocalcemia, even before any radiological changes occur. This would probably explain why radiological changes were observed only in two infants in our series in spite of the presence of the laboratory evidence of vitamin D deficiency in all of them.

The American Association of Pediatrics

has recommended that a reduced dose of 200 units be given to all infants, children and adolescents (9). In the UK, the Department of Health recommends 400 units for the pregnant and lactating women, 340 units for infants under 6 months and 280 units for children under 4 years with no recommendation for older children(10). Greer and Marshal, reported that vitamin D unsupplemented, breastfed infants had no evidence of vitamin D deficiency during the first 6 months of life(11). However, based on observations in Alaska, Gessner, *et al.* concluded that exclusive breastfeeding is a risk factor for vitamin D deficiency in early infancy(12). Recommendations for vitamin D supplementation of all exclusively breastfed infants at an early age and continuation of supplementation throughout the duration of breastfeeding have been made from observations in another study from USA(13).

Our observations suggest that vitamin D deficiency is an important etiological factor for hypocalcemic seizures in exclusively breast fed infants. This study also emphasizes the importance of adequate exposure of sunlight to pregnant women, lactating mothers and infants and also the need for vitamin D supplementation to exclusively breast fed infants.

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