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CASE REPORT

Case series: Vitamin D deficiency in exclusively breastfed term and late preterm neonates

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Abstract:
Vitamin D plays an integral role in calcium metabolism. Vitamin D levels in neonates are determined by in-utero transfer of vitamin D and through breast milk. This in turn depends on the maternal stores of vitamin D. We present case series of term and late preterm neonates who were admitted to tertiary level neonatal ICU with vitamin D deficiency manifesting as symptomatic hypocalcemia.

Keywords: *maternal vitamin D deficiency, neonatal vitamin D deficiency*
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Introduction:

Vitamin D deficiency was believed to be uncommon in tropical countries like India where there is abundant sunlight. However, few studies from North India showed a prevalence of 81-84% of vitamin D deficiency in pregnant mothers [1,2]. The deficiency was attributed to decreased exposure to sunlight due to use of sunscreen and relatively darker skin pigmentation of Indian population.

Vitamin D levels of neonates depend predominantly on the intrauterine transfer from the mother and in the post natal period through the breast milk. Hence, neonates born to vitamin D deficient mothers are likely to have a decreased vitamin D status.

In this case series, we present term & late preterm neonates admitted to neonatal ICU with symptomatic hypocalcaemia due to vitamin D deficiency secondary to maternal vitamin D deficiency.

Clinical manifestations

Term and preterm neonates with various neurological manifestations admitted to NICU were evaluated after taking an informed consent (Table-1) Clinical examination and routine investigations including CSF and neurosonogram were within normal limits. All these neonates were found to have hypocalcemia (Serum calcium <7 mg/dl and serum ionized calcium <4 mg/dl). They were treated with 6-8 ml/kg/day of IV calcium therapy and single dose of intra-muscular Magnesium sulphate (0.2 ml/kg 50% MgSO4). However, even after 48-72 hours, these neonates continued to have persistent hypocalcemia. On further investigations, these neonates had normal serum levels of phosphorus, alkaline phosphatase, magnesium, and

Table 1. Clinical presentation

Case	Age	Day of presentation	Weight (kg)	Mode of presentation
Baby 1	Preterm (35weeks)	5	1.8	Apnea
Baby 2	Preterm (35weeks)	2	1.73	Jitteriness
Baby 3	Term	10	3.4	Seizures
Baby 4	Term	2	3.25	Seizures
Baby 5	Term	5	3.4	Seizures
Baby 6	Term	6	3.45	Seizures
Baby 7	Term	6	3.80	Seizures

parathormone levels. Serum Vitamin D levels (1,25 OH and 25 OH vitamin D3) were done and all these neonates had severe deficiency of vitamin D3 levels (serum vitamin D levels <10 mg/dl). When the mothers of the respective neonates were investigated, they were also deficient in calcium and 25 hydroxyvitamin D3.

Clinical manifestations and biochemical indices of these neonates with their respective mothers' vitamin D levels are given in Table-1 and Table- 2.

The neonates were treated with oral vitamin D3 sachet (60000 IU) per week for 5 weeks and

Table 2. Biochemical indices of patients and their mather.

	Serum Calcium (mg/dl)	Serum Ionized Calcium (mg/dl)	Serum Phosphorus (mg/dl)	Serum Parathormone (mg/dl)	Neonatal Vitamin D (mg/dl)	Maternal Vitamin D (mg/dl)
Reference range	8.4-10.3	4.2-5.1	4-7	11.1-79.50	30-100	30-100
Baby 1	4.2	2.1	8.2	87.7	11	11
Baby 2	7.4	3.77	7.4	85.5	10.7	9.2
Baby 3	7.6	3.4	7.8	109	12	5.6
Baby 4	6.6	3.64	6.7	195	4.61	6.17
Baby 5	7.7	3.86	5.3	98.7	5.07	5.52
Baby 6	5.6	3.19	9.5	115.1	6.42	6.23
Baby 7	6.0	3.01	6.7	90.4	4.76	9.26

rocalterol 0.25mg ¼ sachet daily till the serum calcium was more than 8.5 mg/dl. Treatment was initiated for the mothers too, with oral vitamin D3 (60000 IU) per week for 8 weeks. The laboratory investigations done after 8 weeks showed normal levels of serum calcium and 25 hydroxyvitaminD3 both in the mother and the baby.

Discussion

The present case series included term and late preterm babies exclusively on breastfeeding. Physiologically, in the healthy term neonates too, there is a decline in the serum calcium levels for the first 24-48 hours, the nadir usually 7.5-8.5mg/dl. Thereafter, progressively it rises to the mean values. However, with vitamin D deficiency, the decline in serum calcium levels is accelerated [3].

Vitamin D is synthesised in the skin when its precursor, 7-dehydrocholesterol is exposed to the ultraviolet rays from the sun. This is hydroxylated to 25hydroxyvitamin D in the liver and to 1,25 dihydroxyvitamin D in the kidney which enhances the absorption of calcium predominantly from the intestines and also reabsorption from the kidneys when the serum calcium levels decline.

People living in tropical countries as in India, which extends from 8.4º N latitude to 37.6° N latitude has majority of its population living in areas receiving ample sunlight throughout the year. Hence, it is assumed that these people have less incidence of vitamin D deficiency including pregnant women [4]. But, the amount of ultraviolet exposure available for the synthesis of vitamin D depends on the amount of skin exposed to sunlight especially at noon, amount of skin pigmentation, body mass, degree of latitude, season, the amount of cloud cover, the extent of air pollution, and the extent of UV protection, including clothing and sunscreens [5,6] In the present case series, all the mothers gave history of using sunscreen creams and decreased exposure to sunlight, though we did not calculate the exact sunshine exposure. This could have attributed to vitamin D deficiency seen in these mothers.

There is a close relationship between the maternal and neonatal vitamin D levels. Vitamin D levels in neonates depend on the antenatal transfer of the vitamin from mother and postnatal transfer through the breast milk and exposure to sunlight. Vitamin D in breast milk relates to mothers' vitamin D intake, skin pigmentation and sunlight exposure. This implies that babies born to mothers with vitamin D deficiency are very likely to develop vitamin D deficiency unless supplemented from outside or adequately exposed to sunlight which is often not practical during early infancy.

The breast milk of vitamin D replete mothers contains only about 15-75 IU/L of vitamin D per litre which is insufficient to meet the recommended RDA of vitamin D (400 IU/L) [7-9]. Postnatal exposure to sunlight is an important source of vitamin D synthesis in neonates. Exposure to the sunlight in neonates is unlikely in the early period of life. The above factors discussed could have led to Vitamin D deficiency seen in neonates in this case series.

Most of these neonates had refractory hypocalcemia and did not respond to routine calcium supplementation. This could be explained by the role of vitamin D3 in absorption of calcium.

Though the neonates had different presentations giving a clue to the diagnosis, the mothers were asymptomatic. Our cases are an eye opener to the possibility of higher prevalence of maternal vitamin D deficiency and in turn neonatal vitamin D deficiency in the tropical countries. Term/Preterm neonates presenting as early onset hypocalcemia refractory to treatment should hence be investigated further for associated vitamin D deficiency.

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