

Rickets Presented with Hypocalcaemic Seizures in Infancy: Case Series

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ABSTRACT

Vitamin D Deficiency (VDD) is a serious health issue in Sri Lanka in spite of sun exposure throughout the year.

This is a case series of six infants presented with hypocalcaemic seizures diagnosed to have VDD rickets. They presented at the age of 2 to 5 months, one presented with febrile seizures and the rest had afebrile seizures, in which two had status epilepticus. None of them had clinical features of rickets. All six infants had biochemical and radiological evidence of VDD and rickets. VDD rickets should be one of the differential diagnosis in the evaluation of an infant with seizures. All the pregnant mothers and the infants should be supplemented with vitamin D as recommended by the global consensus to prevent this life-threatening complication.

INTRODUCTION

The Sri Lanka is a tropical country with sun exposure throughout the year. Therefore, VD supplementation has not been introduced into national maternal health programme, the pregnant and lactation mothers only supplement with iron and Calcium. Provided the dark skin, the limited exposure to sun light due to cultural reasons leads to insufficient production of VD and lack of dietary fortification on VD result in VDD. Inefficient supply of VD during the periods of high demand, such as pregnancy and lactation leads to maternal VDD and exclusive breast feeding with VD depleted milk causes VDD rickets and hypocalcaemic seizures in infancy and childhood [1-3].

CASE HISTORY

This is a case series of six infants presenting with hypocalcaemic seizures at 2 to 5 months of age. One presented with febrile seizures and the rest of the five presented with afebrile seizures, while two of them had status epilepticus. None of them had metabolic bony deformities of rickets as metaphyseal widening, frontoparietal bossing, rickety rosary, craniotabes or fractures.

They were term babies born to non consanguineous healthy parents. No history of perinatal complications. Mothers were multiparous with previously healthy children. Two of them were from Muslim community, who cover except face in outdoor limiting the exposure to sun and others were Sinhalese, no particular restriction found for sun exposure. All six infants were mostly kept indoor and well covered when taking

outdoors as a custom, with minimum sun exposure. All were exclusively breast fed and weight gain was satisfactory.

Biochemistry revealed negative septic screen (in febrile convulsion), normal blood sugars, electrolytes, and magnesium levels, renal and liver functions. Cardiac assessment including chest X-ray and echo cardiogram excluded dilated cardiomyopathy in all six infants. All had hypocalcaemia, VDD or insufficiency, high Alkaline Phosphatase (ALP) and High Parathyroid Hormone (PTH) with radiological features of early rickets (Figure 1) (X-ray of two infants with splaying and fraying), confirming the diagnosis of VDD rickets. (Table 1)

Mothers were clinically asymptomatic, having VD insufficiency and normal Ca, phosphate, ALP. They had taken only Ca, without vitamin D supplementations during the pregnancy and lactation. Initially hypocalcaemic seizures were managed with IV Calcium gluconate infusion, Calcitriol and oral Calcium supplementation to bring up the Calcium level to normal range. All the infants were started with therapeutic dose of oral Ergocalciferol 3000 units daily and Ca supplementation continued for three months, followed by maintenance dose of Ergocalciferol 400 units daily. The mothers were given vitamin D and Ca supplementation.

Table 1: Biochemical markers of infants and mothers.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age in months	2	2	4	3	5	3
Sex	Male	Male	Female	Male	Female	Female
Ethnicity	Sinhala	Sinhala	Muslim	Sinhala	Sinhala	Muslim
Presenting complaint	Afebrile convulsions	Convulsions with fever	Afebrile convulsions	Afebrile convulsions	Afebrile convulsions	Afebrile convulsions
Calcium (2.2–2.7 mmol/l)	0.85	1.68	1.3	1.3	1.1	1.4
Phosphate (1.45– 2.0 mmol/l)	1	1.3	1.22	1.4	1.2	1.29
ALP (60 -425 iu/l)	812	1211	1306	550	620	1507
PTH (10 -65 pg/ml)	120	170	199	68	97	82
Magnesium (0.6-1.0 mmol/l)	0.8	0.9	1.1	0.8	0.7	0.7
Infant 25-hydroxy vitamin D level (sufficient >50 nmol/l)	11	27	38	24	21	26
Parity	P3C3	P2C2	P5C5	P3C3	P3C3	P4C3
Maternal 25-hydroxy vitamin D level (sufficient >50 nmol/l)	46	48	45	46	40	35



Figure 1: X- ray hand of two infants with splaying and fraying.

DISCUSSION

VDD rickets is defective ossification and mineralization of growth plate of bone in children mainly due to VDD, with or without inadequate dietary Ca intake. We defined levels for VD, assuming VDD causes impaired bone mineralization and VD insufficiency causes non-skeletal manifestation other than defective bone mineralization. The serum 25-hydroxy vitamin D level below 30 nmol/l (12ng/ml) is defined as VDD, 30-50 nmol/lis VD insufficiency, and if the level above 50nmol/l (20ng/ml) VD sufficiency [4]. However, defining the cut-off numbers for VDD and insufficiency is controversial, since the skeletal manifestations depend of dietary Ca intake, individual sensitivity and metabolism of VD and Ca [5].

There are two types of VD, D₂; Ergocalciferol, produced by plants and D₃; cholecalciferol, product of VD in the skin. The main product of VD in humans is D₃. In the presence of Ultraviolet B (UVB) 290- 315nm range, 7-dehydrocholesterol is converted to D₃ in the skin and transport to liver that converts 25-OH-VD by 25- hydroxylase [5]. The active VD is 1, 25-dihydroxy vitamin D, the product of second hydroxylation by 1- hydroxylase in the kidneys [6]. In spite of plenty of sun light in tropical countries, melanin in the dark skin acts as a barrier for UVB, a dark skinned person needs 5 times more exposure to sun light than a white skinned to produce equal amount of VD.

VD affects the function of many other organs including dysfunction of innate immunity, decrease latency of malignancies, dysregulation of autoimmunity and myocadiac dysfunction leading to dilated cardiomyopathy and heart failure, therefore VDD has devastating effect of human body [1,4,6]. Rickets is an extreme form of VDD manifestation, seen all over the world and the peak incidence occurs at the age of 3- 18 months [6].

Asymptomatic VDD and VD insufficiency is common in pregnant and lactating mothers in Asian and African ethnicity, especially with insufficient exposure to sun-light and co existing lack of dietary supplementation [7]. If the mother is VDD or insufficient, their breast milk VD content is not sufficient to provide the requirement of the new-born or the infant [1,3,7]. In this study population, the 25 hydroxy VD level of the mothers were measured at the time of the presentation of the infant with seizures, therefore 1 to 4 months after delivery, therefore not

an accurate reflection of the VD status during the pregnancy and necessarily not a reflection of VD status of the infant since the breast milk is poor source of VD. This might explain the relatively better VD status in the mother's comparative to the infants in the study group.

The VD supply in breast milk is not sufficient to provide the demand of the growing bones in infancy [2-4]. Therefore the recommendation is to supplement pregnant and lactating mothers with 200 –400 iu and the breast feeding infants, the non-breast feeding infants who ingest less than 1 litre of VD fortified formula and children and adolescence who takes less than 400 iu of VD by food should have 600 iu per day of VD supplementation regularly [4,6]. Considering the increase demand of vitamin D during pregnancy and lactation, many studies have proven the pregnant and lactating mothers need higher dose of vitamin D supplementation like 1000- 1600 iu, in spite of the recommended Daily Intake Requirement (DIR) of 400 iu for a healthy adult [2-4].

CONCLUSION

VDD rickets in infancy can present with hypocalcaemic seizures without any other clinical features, which should be considered in the evaluation of an infant with seizures. Even in tropical countries like Sri Lanka, all the pregnant and lactating mothers and the infants should be supplemented with VD as recommended by the global consensus recommendations on prevention and management of VDD Rickets.

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