

# Congenital rickets due to maternal vitamin D deficiency: a case report

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## Abstract

**Objective:** Rickets due to vitamin D deficiency is an important cause of the infantile hypocalcemia, but congenital rickets is not so common. Vitamin D deficiency may present with hypocalcemia and sometimes with hyperphosphatemia because of the inadequate response of parathyroid hormone to hypocalcemia during early infancy. We report a case of congenital rickets due to maternal vitamin D deficiency.

**Case:** The patient was admitted with hypocalcemic seizure at 10 days of age. Both the baby and her mother had low 25(OH) vitamin D3 levels.

**Conclusion:** Vitamin D deficiency should be considered primarily in the differential diagnosis of neonatal hypocalcemia, particularly in those areas where maternal vitamin D deficiency is common.

**Key words:** Vitamin D, rickets, newborn.

## Maternal D vitamini eksikliğine bağlı konjenital rikets: Olgu sunumu

**Amaç:** D vitamini eksikliğine bağlı rikets erken bebeklik döneminde görülen hipokalseminin önemli bir nedenidir. Ancak konjenital rikets çok sık değildir. D vitamini yetersizliği hipokalsemiye parathormon cevabının yetersiz olması nedeniyle sıklıkla hipokalsemi ve nadiren de hiperfosfatemiyle kendini gösterebilir. Bu makalede, maternal D vitamini eksikliğine bağlı bir konjenital rikets olgusu sunulmaktadır.

**Olgu:** Hasta 10 günlükken hipokalsemik nöbet geçirme öyküsü ile polikliniğe getirildi. Hem bebek hem de annede 25(OH) vitamin D3 düzeyi düşük olarak saptandı.

**Sonuç:** Maternal D vitamini eksikliğinin sık olduğu bölgelerde neonatal hipokalsemi ayırıcı tanısında D vitamini eksikliği öncelikle düşünülmelidir.

**Anahtar sözcükler:** D vitamini, rikets, yenidoğan.

## Introduction

Vitamin D deficiency is an essential public health issue since mothers in Turkey, especially in eastern cities do not receive sufficient vitamin D support, and insufficient sunlight exposure.<sup>[1]</sup> In a study performed by Özkan et al.<sup>[2]</sup> in 1998, it was found that rickets incidence due to vitamin D deficiency among children (ages 0-3) was 6.09%. Ministry of Health initiated the project of "Prevention of Vitamin D Deficiency and Protection of Bone Health" in 2005 in order to eradicate rickets due to insufficient vitamin D intake.<sup>[3]</sup> Within the context of this project, vitamin D with the dose of 400 IU/day is given for free to all infants in health centers. The project

was considered to be effective, so it was decided to extend the project as covering pregnant in order to prevent maternal/perinatal vitamin D deficiency. In 2011, "The Program of Vitamin D Support for Pregnants" was initiated. Within the context of this program, it is recommended to give vitamin D support (1200 IU/day) to all pregnant and also mothers after delivery without making discrimination except the cases where vitamin D cannot be applied.<sup>[4]</sup> On the other hand, American Congress of Obstetricians and Gynecologists (ACOG) reports that there is no satisfactory evidence for screening all pregnant in terms of vitamin D deficiency, and only pregnant under risk may be researched. It is

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reported that vitamin D support in the dose of 1000-2000 IU/day will be sufficient when vitamin D deficiency is detected during pregnancy, and that more studies are required to determine whether higher doses are harmful or not.<sup>[5,6]</sup>

Requirement of vitamin D support and the dosage may vary according to countries and regions. In Turkey, despite the improvements in public health field, clinical problems due to vitamin D deficiency still maintain their importance. Clinical and radiological findings may be unclear in rickets cases seen in newborn and early infancy, and the disease may appear only by hypocalcemia (and sometimes by hypocalcemic seizure).<sup>[6]</sup> Therefore, it is recommended to evaluate children for rickets findings who refer to hospital during their first three years in socio-economically low level regions, and to confirm diagnosis by radiological and biochemical findings under suspicious cases.<sup>[1]</sup> Hypotonia, craniotabes, tremor episodes, high level of serum alkaline phosphatase, low level of serum 25(OH) vitamin D3, secondary hyperparathyroidism, hypocalcemia, and persistent convulsion due to calcemia can be seen in congenital rickets. In these cases, hypophosphatemia, normophosphatemia or hyperphosphatemia may accompany to hypocalcemia in addition to classical rickets laboratory findings.<sup>[6]</sup> In such cases, there may be problems in differential diagnosis. In this article, we have presented a case with hypocalcemic seizure history at 10 days of age and who received congenital rickets diagnosis during the follow-up in the light of literature.

## Case Report

A girl baby at ten days of age was referred to Pediatric Emergency Service with complaints of contraction at arms and legs and hiccup. It was stated that contractions started three days ago and the frequency of contractions increased gradually. It was also reported that the baby was delivered by normal vaginal delivery at 38 weeks of gestation and in 2880 g weight, and that she cried when born and there was no problem after delivery.

By the history, it was understood that the mother regularly went for checks during pregnancy, and there was no health problem; however, she did not take iron and vitamin support as recommended. The mother who was a house-wife had a veiled dressing style. On the other hand, she indicated that she tried to benefit from sun. There was no kinship between mother and father. The baby was fed only by breast milk.

In the physical examination, body weight was measured as 3100 g, height as 54 cm, head circumference as 34 cm, peak heart rate as 138/min, and respiratory rate as 32/min. Newborn reflexes of the cases was vivacious, and her muscle power and tonus were normal. Pathological reflex was not evaluated. Frontal fontanel was 2x2 cm and in normal curve. The systemic examination indicated no significance except icterus, and short systolic murmur at 1/6 rate on the left side of sternum. Respiratory support was applied to patient who had convulsive seizure, and vascular access was opened. Intravenous midazolam was carried out, and oral phenobarbital was applied. Although the seizure was taken under control, it started again. Upon the detection of hypocalcemia [serum calcium 6.4 mg/dl (8.6-10.8)] in the initial evaluation, IV calcium gluconate (10%, 2 ml/kg) was applied and the seizure ended. Then, calcium gluconate infusion (10%, 200 mg/kg/day) and vitamin D (400 IU/day) were initiated.

According to other laboratory evaluations, full blood count was normal, blood glucose level was 80 mg/dl (70-120), serum total bilirubin was 11.9 mg/dl, direct bilirubin was 0.5 mg/dl, albumin was 3.4 g/dl (3.4-4.8), phosphorus was 10.3 mg/dl (2.7-6), magnesium was 0.57 mmol/l (0.7-0.9), and alkaline phosphatase (ALP) was 178 U/L (0-400). Cerebrospinal fluid (CSF) and urine examinations, blood and urine amino acid levels, cranial screenings were normal. There was no growth in CSF, urine and blood cultures. On the 7th day of hospitalization, 50% MgSO<sub>4</sub> as 0.2 ml/kg/dose was added to the treatment due to the presence of intermittent contractions, persistence of hypocalcemia (6.8 mg/dl), and the detection of hypomagnesemia. In addition, the dose of vitamin D was increased to 2000 unit/day. On the 4th day of this application, serum calcium level was 8.2 mg/dl, and magnesium level was 1.02 mmol/L; oral calcium lactate treatment (0.5 g/kg/day, 4 doses) was started and magnesium treatment was terminated. Parathormone (PTH) level checked for hypocalcemia etiology was found as 90 pg/ml (11-67), and 25(OH) vitamin D3 level was found as 10.3 µg/l. According to hospital laboratory standards, <10 µg/l was displaying severe vitamin D deficiency. The mother was also checked simultaneously and it was found that serum calcium level was 8.9 mg/dl, phosphorus was 3.1 mg/dl, magnesium was 0.87 mmol/l, ALP was 81 U/L, PTH was 70 pg/ml, 25(OH) vitamin D3 level was 7.8 µg/l and HbA1c was 5.9%.

Osteoporosis was found in the bone mineral densitometer analysis (T score ≤2.6). The mother was referred

to gynecology and endocrinology clinics. The echocardiography displayed no significance except patent foramen ovale. In the radiological examinations, chest x-ray was interpreted as normal; however, pseudoglaucous cupping was found in the distal metaphysis of ulnar bone in the left hand-wrist radiography (**Fig. 1**). When the history was investigated deeply upon these findings, it was found out that the family was living in shanty-house, the mother spent most of her pregnancy within the house, she took her vitamin drugs in the beginning as recommended by her doctor, but she stopped to take them after third month due to adverse effects (nausea, stomachache). Congenital rickets due to maternal vitamin D deficiency was considered in the case.

No seizure and contraction was observed in the follow-up. Electroencephalography was evaluated as normal and phenobarbital was stopped by reducing. Due to low level of calcium (<8.6 mg/dl) and high level of phosphor (>8 mg/dl) observed in the follow-up, calcitriol (125 ng/kg/day) was added to the treatment. Then the calcitriol dose was increased (250 ng/kg/day) since there was no response. The levels of serum calcium, magnesium, phosphor, ALP, 25(OH) vitamin D3 and PTH levels measured on the 29th day of the hospitalization was 10.6 mg/dl, 1.02 mmol/L, 6.9 mg/dl, 300 U/L, 24.6 µg/l and 35.1 pg/ml, respectively. The patient was discharged on the 31st day of the hospitalization while she was still using oral calcium lactate (100 mg/kg/day) and

calcitriol (250 ng/kg/day). It was suggested to take 400 IU/day vitamin D. In the clinical follow-up, her oral calcium lactate and calcitriol treatment was stopped by reducing. On the follow-up of the case, her clinical and laboratory evaluations and neural-development were found to be normal on the check performed on 3rd month.

## Discussion

There are two types of hypocalcemia in newborns which are early types occurring in the first three days of life and late types occurring after 5th-7th days. The reason of early neonatal hypocalcemia can be the low level of post-natal physiological calcium as well as prematurity, perinatal asphyxia, maternal diabetes, hypoparathyroidism, and maternal hyperparathyroidism. Late neonatal hypocalcemia may be caused by nourishment with high phosphate contents, intestinal calcium malabsorption, hypomagnesemia, maternal hyperparathyroidism, and maternal vitamin D deficiency.<sup>[6,7]</sup>

In this case, conditions observed at late neonatal period were analyzed. ALP level was normal, 25(OH) vitamin D3 level was low, and PTH level was high at limit in addition to hypocalcemia, hyperphosphatemia, and hypomagnesemia. Simultaneous 25(OH) vitamin D3 level of mother was low and PTH level was at upper limit. It was considered that the normal level of ALP might be secondary to hypomagnesemia, and zinc deficiency nutritionally may accompany due to the fact that ALP enzyme is a zinc-dependent enzyme.

In fetal life, the most significant source of vitamin D is mother. At postnatal period, the amount of vitamin D becomes important which comes by breast milk and develops on skin by sunlight. Vitamin D can easily pass through placenta especially after 2nd trimester. Vitamin D level in cord blood is also closely associated with maternal vitamin D condition [25(OH) vitamin D3].<sup>[6,8]</sup> Studies performed in many countries confirm the relationship between mother and baby for 25(OH) vitamin D3 level, and these studies show that vitamin D insufficiency seen in early infancy starts in intrauterine period.<sup>[8]</sup>

The studies performed in Turkey show that mothers and babies have a life which is poor in terms of vitamin D.<sup>[9-14]</sup> In the study performed by Andiran et al.,<sup>[15]</sup> it was found that the most significant risk factor for low level of 25(OH) vitamin D3 was maternal 25(OH) vitamin D3 level below 10 ng/ml. In the mother of our case, 25(OH) vitamin D3 level was significantly low (7.8 µg/l).



**Fig. 1.** X-ray of infant's wrist.

The transition from the first phase [the period in which 25(OH) vitamin D<sub>3</sub> level and intestinal calcium and phosphor absorption decrease] of vitamin D deficiency to second phase [the period in which serum calcium is normalized by calcium mobilization through bones by the influence of PTH and 1,25(OH)<sub>2</sub>] may be delayed at postnatal period. Therefore, these cases may apply for hypocalcemia. In newborn period, renal phosphor discharge is low due to immature PTH response; for that reason, it is not a surprise to observe normophosphatemia and hyperphosphatemia. Thus, it was found out that 35% of the cases were hyperphosphatemia in the beginning in a study where 42 infantile rickets cases were analyzed.<sup>[16]</sup>

In our patient, hypoparathyroidism / pseudohypoparathyroidism diagnoses were ruled out since hypocalcemia was recovered, phosphor level decreased, and PTH level was at normal limits in the follow-up; and it was considered by the examinations during admission that hyperphosphatemia accompanying to hypocalcemia was associated with insufficient PTH response.

There is no consensus about the dose of vitamin D to be given to pregnant, and dosage varies according to countries. Congenital rickets treatments associated with maternal vitamin D deficiency also differ. Cases treated by high dose of vitamin D (5000 IU/day) were reported in the literature.<sup>[17]</sup> In our case, it was preferred to start with low dose of vitamin D in the beginning and to increase gradually, and to give active vitamin D when it was not efficient.

## Conclusion

Although it is considered that maternal vitamin D deficiency may be seen in mothers who have veiled dressing style and do not benefit from sunlight sufficiently, there is no study proving this assertion. It is also a fact that a significant distance has been covered by the campaigns run by the Ministry of Health in order to prevent infantile rickets. Since vitamin D addition to newborns is done after 15th day, it should be remembered that there is a risk to see congenital rickets unless sufficient vitamin D support is provided to pregnant.<sup>[8]</sup> It is important to carry out regular gestational follow-ups, and to evaluate whether vitamin preparates are used in physician checks properly or not. In our country, congenital rickets also should be kept in mind in differential diagnosis for newborns referring with convulsion.

**Conflicts of Interest:** No conflicts declared.

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