The relationship of hypocalcemic convulsions related to nutritional rickets with age, gender, season, and serum phosphorus levels

Zafer Bicakci, *MD.*

ABSTRACT

Objective: To retrospectively evaluate the epidemic characteristics of children with hypocalcemic convulsion related to nutritional rickets in the province of Kars, Turkey.

Methods: In this study, clinical and laboratory findings of 93 infants, aged between 1-24 months, who were diagnosed as hypocalcemic convulsive resulting from nutritional rickets between January 2000 and June 2005 in Kars Maternity and Child Hospital, were investigated. The data of the cases with hypocalcemic convulsive rickets were collected from the hospital archive file.

Results: The mean and median ages of the cases were 8.93 and 6 (1-24) months, and 66 (71%) were male. Most of the patients were admitted to hospital in February and March, whereas 46% were admitted in winter, 44% in spring, 8% in autumn, and 2% in summertime. Serum calcium levels of all cases were low (mean: 5.4 ± 0.84 mg/dl) and serum alkaline phosphate levels were high (mean: 1286 ± 528 IU/L), while serum phosphorus levels were low in 19 (20.4%), high in 8 (8.6%), and normal in 66 (71%) patients.

Conclusion: While evaluating the causes of convulsion, hypocalcemic convulsion related to nutritional rickets should be considered among the causes as well as age, gender, and season of the year, and diagnosis, and treatment should be initiated without delay. In addition, serum phosphorus level should also be questioned in the diagnosis of nutritional rickets.

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From the Department of Pediatrics, Faculty of Medicine, Kafkas University, Paşaçayır Mah, Kars, Turkey.

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Address correspondence and reprint request to: Dr. Zafer Bicakci, Assistant Professor, Department of Pediatrics, Faculty of Medicine, Kafkas University, Paşaçayır Mah, Kars, Turkey. Tel. +90 (474) 2127915. Fax. +90 (474) 2120996. E-mail: zaferbicakcib@yahoo.com.tr

It has been recently reported that nutritional rickets is still an important health issue that affects infants with a frequency up to 19% in Turkey.[1] Vitamin D deficiency constitutes a major problem in the rural areas of our country, mainly Eastern and Southeastern Anatolia; however, unnecessary administration of vitamin D to infants in big cities has emerged as another issue.[1] Clinical findings of rickets related to vitamin D deficiency varies among different age groups. In the early infancy periods, patients may mostly present to hospitals with suspected hypocalcemic convulsions. Hypocalcemic convulsions secondary to rickets are rare in developed countries. It has been reported that 55-75% of nutritional rickets cases are male, and 25-45% are female, and that they are mostly diagnosed in spring and winter during the fast growing period of infants between the 3rd and 36th months of development, and even earlier for preterm infants.[2-6] To make an epidemiological evaluation of nutritional rickets in society is expensive, and also requires a good deal of experience. Due to the compulsory transportation of the patients to the emergency service with hypocalcemic convulsion related to nutritional rickets, an epidemiological (except frequency) evaluation of nutritional rickets in society is an objective criterion of hypocalcemic convulsions. This study aims to evaluate the clinical, laboratory, and epidemiological characteristics of infants with hypocalcemic convulsions from rickets in the northeast region of Turkey.

Methods. In this study, clinical and laboratory findings of 93 infants, aged between 1-24 months, who were diagnosed with hypocalcemic convulsions resulting from nutritional rickets between January 2000 and June 2005 in Kars Maternity and Child Hospital, were investigated. Official permission was obtained from the hospital authorities before starting the study. The data of the cases with hypocalcemic convulsive rickets were collected from the hospital archive file. Hypocalcemic convulsion and rickets were diagnosed according to the following criteria: hypocalcemia detected after generalized convulsions, high alkaline phosphatase levels, craniotabes, rachitic rosary,

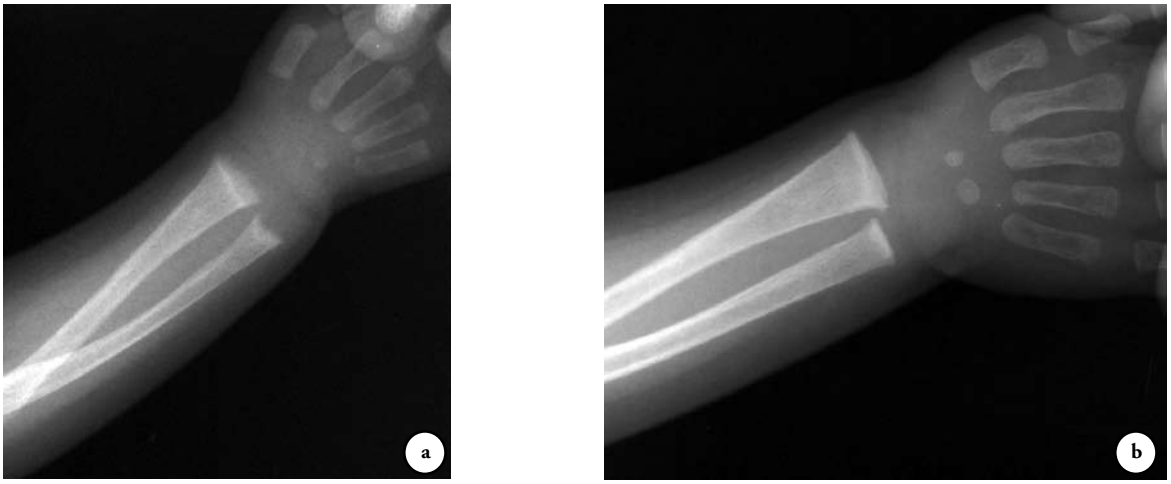

Figure 1 - Anteroposterior wrist radiographs of an infant with rickets **a**) prior to, and **b**) 3 weeks after treatment.

and widening of the wrist on physical examination, and widening or brush-like appearance on the lower end of the radius and ulna in anteroposterior radiography of the wrist. Patients whose history, clinical, radiological, and other laboratory findings did not confirm nutritional rickets and who had convulsions without hypocalcemia were not included into the study. A dose of 300,000 U vitamin D3 was administered orally at 2-hourly intervals for 6 hours to the subjects. Ca-gluconate 10% in 4 doses at 0.5-1ml/kg, and 0.3 mg/kg diazepam were given for convulsions; 5 mg/kg/day phenobarbital was occasionally initiated for recurrent convulsions. It was observed that calcium levels returned to normal generally within 2-4 days. Improvement was proven radiologically, demonstrating the calcification line on anteroposterior wrist radiographies of the subjects obtained 20-25 days later (**Figures 1a & 1b**). The age average of the cases was applied in accordance with Kolmogorov-Smirnov test.

Results. Of 93 infants, 66 were male (71%) and 27 female. The mean and median of ages were 8.94 (ranged 1-24 months) and 6 months, (**Table 1**). Most of the patients, namely, 46%, were admitted to hospital in winter, whereas 44% were admitted in spring, 8% in autumn, and 2% in summer (**Table 2**). Most of the mothers were dressed in traditional clothes only with their faces and hands uncovered. None of the mothers used vitamins during their pregnancy history. Fifty-six (60.2%) infants were breast-fed only, 9 infants (9.6%)

Table 1 - Distribution of the subjects according to age.

Age (months)	Cases
1	3
2	1
3	4
4	10
5	12
6	14
7	11
8	9
9	7
10	6
11	5
12	5
14	1
18	2
24	3

Table 2 - Distribution of the month of presentation to hospital.

Months	Cases
September	0
October	2
November	5
December	4
January	15
February	24
March	25
April	13
May	3
June	1
July	0
August	1

Table 3 - Physical findings of 93 subjects.

Findings	n (%)
Craniotabes	51 (54.8)
Anterior fontanel bulging	7 (7.5)
Caput quadratum	25 (26.8)
Sweating on the neck	60 (64.5)
Harrison's groove	14 (15)
Inspiratory stridor	3 (3.2)
Widening in wrists	60 (64.5)
Rachitic "rosary"	85 (91.3)
Others	13 (13.9)

were given only cows milk, 4 (4.3%) infants were breast-fed and given cow's milk, 5 (5.3%) infants were breast-fed and given formula, and 19 (20.4%) were breast-fed, and given formula and cow's milk. Forty-seven (50.5%) of the infants generally remained indoors at home. The rest of the infants went outside occasionally without any purpose to get sunlight. None of the infants had any history of regular use of vitamin D. Physical findings related to the infants is shown in **Table 3**. Serum calcium levels of all infants were lower (average 5.4 ± 0.84 mg/dl) than normal limits (8.8-10.8 mg/dl). Serum alkaline phosphatase levels were higher (average 1286 ± 528 IU/L) than normal limits (145-420 IU/L) in 91 (97.8%) infants, and normal in 2 (2.2%) infants. However, serum phosphorus levels were found to be low in 19 infants (20.4%), high in 8 infants (8.6%), and normal in 66 infants (71%) (normal phosphorus limits are 3.8-6.5 mg/dl).[7]

Discussion. Although rickets related to vitamin D deficiency has been almost eliminated in developed countries, it can be seen in the immigrants, and it continues to be an important health problem in developing countries.[2,5,6,8-13] It has been reported that hypocalcemic convulsions resulting from vitamin D deficiency are also seen in developed countries.[6,8-13] Studies performed in our country, revealed that the frequency of rickets is up to 19% with regional and nutritional differences.[1] In a study,[4] which investigated children between 0-3 years of age, diagnosed with rickets in Erzurum, they found that 6.8% of the cases were admitted with hypocalcemic convulsions. In another study performed by the same center,[3] vitamin D deficiency was detected in early infancy (32-112 days), and demonstrated that 78.7% of the cases were admitted to hospital with suspected hypocalcemic convulsion. Therefore, hypocalcemic convulsions stemming from nutritional rickets and seasons, age, and gender is a more objective finding than other clinical signs and symptoms of rickets.

Vitamin D deficiency-related rickets is mostly seen during the period from the first 3-4 months of fast growth to 3 years, and is even earlier for preterm babies, and in newborns of mothers with osteomalacia problems.[4,6,8,11] It has been reported that hypocalcemic convulsions due to rickets are seen most frequently between 4 to 36 months. In one study carried out in Erzurum,[3] hypocalcemic convulsion was observed in 33 (78.7%) out of 42 cases diagnosed as rickets during the early infancy period. However, in another study carried out in Sidney,[6] it was reported that hypocalcemic convulsions were present in most cases under 6 months of age. Although most of our subjects were approximately 6 months old, 8 (8.6%) were younger than 4 months, and none of our infants were older than 24 months.

A study performed in Nigeria[14] revealed that 75% of the rickets cases were male. This number was 63% in a study performed in Tehran,[15] 55% in the Catalonia region in Spain,[2] 67% in Sydney,[6] and 64% and 60% in 2 studies performed in Erzurum at 5-yearly intervals.[3,16] In the present study, 66 (71%) of our cases were male, and 27 (29%) were female. This difference between genders may be related to genetic factors, and the inhibitory effect of estrogen on calcium resorption in bones. Maternal vitamin D deficiency is common among women who are veiled due to cultural/religious reasons and harsh climatic conditions, and women who spend most of the day at home.[3,8,11] In our country, inadequacy of sunlight, and vitamin D supplementation, as well as maternal vitamin D deficiency are major factors in the development of vitamin D deficiency.[3] It has been reported that although the cases of rickets are generally seen in winter and spring, they maybe sometimes seen in autumn.[2] In studies performed in Sydney[6] and Erzurum,[4] rickets was reported to be experienced most frequently in spring and winter. Among our subjects, 46% were admitted in winter, 44% in spring, 8% in autumn, and 2% in summer. Given that hypocalcemic convulsions stemming from vitamin D deficiency is seen most frequently in February and March, and in infants younger than 6 months, it can be concluded that patients are usually born in summer and autumn. Due to traditional/cultural reasons, newborn babies are not taken out of the home, therefore, babies born at the end of summer do not benefit from sunlight before May-June of the following year due to the early cooling of the weather in our region as a result of harsh climatic conditions. In addition to insufficient sunlight and maternal vitamin D deficiency, malnutrition during the weaning and lack of vitamin D support leads to nutritional rickets.

In the diagnosis of rickets, serum calcium level is expected to be normal or low, alkaline phosphatase is high, and serum phosphorus levels are anticipated to be low and less than 4 mg/dl, as well as history, physical examination, and radiological findings.[5] In a study performed in Sydney,[6] all the 11 rickets patients younger than 7 months of age were reported to have hyperphosphatemia. In our country, if alkaline phosphatase is particularly high in subjects with hypocalcemia in early infancy, vitamin D deficiency has to be investigated even if the initial phosphorus level is normal or high.[1] The serum phosphorus level of our subjects was mostly normal (71%), however, it was high among 8.6% of the subjects, and low in 20.4%. The serum phosphorus level was low mostly in patients in the 8-24 month age group. These results suggest that low levels of serum phosphorus are diagnostic in nutritional rickets only up to 20% after 8 months of

age, and that it cannot be used as a criterion for 80% of the subjects. To use this finding as a diagnostic factor, normal intervals should be determined according to age (month) groups. Our 8 cases with high serum phosphorus levels were aged between 2-5 months. In the previously reported studies including 3 and 11 cases, concomitance of hypocalcemia, hyperphosphatemia, and secondary hyperparathyroidism was suggested to be related to parathyroid hormone (PTH) resistance, and hyperphosphatemia was reported to be an expected result in congenital rickets cases, since low PTH response is immature and renal excretion of phosphorus is low in the newborn period. It was also noted that phosphorus levels might be normal or high in early rickets despite the presence of secondary hyperparathyroidism.[3,6] Generally, serum phosphorus level is a weak indicator for the diagnosis of vitamin D deficiency in very young infants. In hypocalcemia subjects in early infancy, vitamin D deficiency must be evaluated regardless of serum phosphorus levels, especially when alkaline phosphatase is high. High levels of serum phosphorus may be related to immaturity in the physiological development of renal functions and response to PTH, and the use of serum phosphorus level as a criterion in the diagnosis of nutritional rickets must be studied extensively.

In conclusion, age, gender, and season of the year should be taken into consideration while evaluating the causes of convulsion, and hypocalcemic convulsion stemming from nutritional rickets should be suspected, and diagnosis and treatment should begin immediately. In addition, the use of serum phosphorus levels as a diagnostic factor in nutritional rickets should also be studied. This study is limited to Kars Province in Turkey, and cannot be considered relevant to all of Turkey.

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