Early and severe presentation of vitamin D deficiency and nutritional rickets among hospitalized infants and the effective factors

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Nutritional rickets is re-emerging as a significant health problem among children. We determined the frequency of nutritional rickets and vitamin D deficiency among hospitalized children and the effective factors. During a one-year period, 305 hospitalized children (ages between 0 to 3 years) were evaluated for clinical and biochemical markers of vitamin D deficient rickets and related factors. Twenty-one of them (6.8%) were diagnosed as nutritional vitamin D deficiency and rickets. Most of the children diagnosed were under one year old (16/21, 76.2%). Fourteen vitamin D deficient rachitic children were admitted to the hospital with infectious conditions, and most of them were respiratory tract infection. The rachitic group was compared for statistical significance with the non-rachitic control patients for the data collected. Rachitic children had a lower rate of vitamin D intake. The frequency of malnutrition and anemia and the percentage of covered mothers were higher in the rachitic group than in the control group. Vitamin D deficiency-related rickets is still a common and serious health problem especially in the infancy period. To address this problem, a specific attention should be given to women of reproductive age and in the early infancy period. Initiation of vitamin D supplementation could be offered very early (perhaps after the birth) in children with risk factors.

Key words: nutritional rickets, children, vitamin D deficiency.

Nutritional rickets maintains its importance in many developing and underdeveloped countries around the world. Although rickets was thought to be completely eradicated in developed countries, recent reports of cases from Canada and the United States have implicated the importance of vitamin D deficiency and nutritional rickets. Vitamin D deficiency is re-emerging as a significant health problem, especially among pregnant women and their infants. Vitamin D deficiency not only causes rickets, but it is also one of the predisposing factors for osteoporosis, cardiovascular disease, multiple sclerosis, and rheumatoid arthritis among adults.

The frequency of this disease varies by age, climate, socioeconomic status of the population and on traditional practices. In our country, rickets due to vitamin D deficiency is not a rare condition since daily diets of newborns and exposure to sunlight are often not sufficient in children.

We aimed in this study to determine the frequency of rickets among hospitalized children who were presented to the Department of Pediatrics in a research hospital in the capital city of Ankara over a one-year period.

Material and Methods

Three hundred and eight children, between 0 to 3 years of age, who were hospitalized in the Ministry of Health, Ankara Education and Research Hospital, Department of Pediatrics because of varying problems over a one-year period (January 2002 - January 2003) were
evaluated. The patients who were diagnosed with rickets due to nutritional vitamin D deficiency were included in the study group.

Age, gender, etiology of admission, infant feeding practice, vitamin D intake history, and outdoor clothing habit of the mother were recorded. The diagnosis of rickets was based on the clinical, radiological and biochemical findings. According to the Centers for Disease Control (CDC), vitamin D deficient rickets has been defined as having a low serum 25-hydroxy-vitamin-D level combined with one or more of the following radiographic changes: osteopenia, widening of growth plates, fraying and cupping of the metaphysis, and craniomalacia. Low serum phosphorus (P) level, normal or low calcium (Ca) level, and significantly high alkaline phosphatase (ALP) levels are also considered as required biochemical criteria for the diagnosis. The presence of clinical signs including craniotabes after four months of age, caput quadratum, wide anterior fontanel, O/X bain of the legs, rosary beads, and Harrison's groove of the chest was recorded. The biochemical evaluation was done according to the criteria described by Fraser et al. Radiologically, the widening of the wrist and cupping and fraying of the ends of the radius and ulna were accepted as pathological findings.

The patients with other causes of rickets such as resistance to vitamin D or vitamin D dependent rickets, anticonvulsant drug usage, or hepatic and renal tubular failure were excluded from the study. One patient with cystinosis, one with tyrosinemia, and one with anticonvulsant medication were excluded. The control group consisted of the 284 non-rachitic children remaining.

Biochemical and hematological parameters were analyzed on admission to hospital. Serum Ca, P and ALP levels were measured by using Bayer Corporation Device® and ADIVA® analyzer. Blood count and peripheral smear were performed in all cases cytometrically by Coulter Gen-S Device®. Serum 25(OH)D₃ levels were determined in the cases diagnosed as rickets. In our hospital, we were not able to measure parathyroid hormone (PTH) levels in all patients. Prior to enrolment in the study, an informed consent was obtained from the patient and his/her parents or local guardian and the study was approved by the Local Ethics Committee.

The children with malnutrition were grouped with respect to the criteria of Gomez et al. Cases diagnosed as nutritional rickets were treated with oral 100,000 U vitamin D₃ every 2 hours, with total dosage of 300,000 U vitamin D₃. Intravenous calcium gluconate (10%, 1 ml/kg) was given for 3 days to the cases whose serum Ca levels were below 7 mg/dl and/or if hypocalcemic symptoms were present. After intravenous therapy, Ca intake was supported by oral Ca lactate therapy.

The rachitic group was compared with the age-matched non-rachitic children as the control group. All cases were evaluated for the parameters such as severity of illness, clinical status, nutritional status, vitamin D intake, breast feeding duration and clothing habit (covered or not) of their mothers.

**Results**

Three hundred and eight patients, aged between 0-3 years, were hospitalized during the study period. Thirteen boys (62%) and eight girls (38%), totally 21 children, were diagnosed as nutritional vitamin D deficient rickets within this group. Three patients had been diagnosed as rickets with secondary causes, and these patients were excluded from the study. Sixteen of the 21 patients (76.2%) diagnosed as vitamin D deficient rickets were under one year old (Fig. 1). The mean age was 9.47±6.46 months.

![age distribution of rachitic cases](image)

**Fig. 1.** Distribution of patients according to ages.

Vitamin D deficient rickets in our patients were found to be nutritional in origin. Fourteen rachitic children were admitted to hospital with infectious conditions, most of which were respiratory tract infection (n=10) (Table I).
On physical examination, persistence of craniotabes after 4 months of age was the most frequent clinical finding (38%, 8/21 of the patients). Widening of wrist (28.5%), asymmetry of the head (19%), and rachitic rosary (14.2%) were other common findings of rickets. The serum Ca levels were low (<8 mg/dl) in 10 children and 6 of them presented with convulsion due to hypocalcemia. The mean Ca level of the study group was 7.41±1.54 mg/dl, mean P level was 4.98±2.5 mg/dl, and mean ALP level was 462±335 U/L (Table II). 25(OH)D₃ levels were low in all rachitic patients (8.3±4.1 µg/L, N: 20-60 µg/L).

Regarding the biochemical stages, of the 21 cases, 10 (47.6%) were in Stage I, 4 (19%) were in Stage II, and 7 (33.3%) were in Stage III. While only 5 patients in the vitamin D deficient rickets group had been reported to have regular vitamin intake and 16 of them (76.1%) had never used oral vitamin D, this ratio was lower (101 children; 35.5%) in the control group (p<0.05).

The percentage of rachitic children with covered mothers because of religious beliefs was 17/21 (80.9%), while the percentage of covered mothers in the non-rachitic cases was 163/284 (57%). When the duration of breast feeding was evaluated, 3 cases (14.2%) had never received breast milk and 7 cases (33.3%) were breast-fed for less than 6 months. Twelve of 21 rachitic children (57.1%) were in the weaning period. Within the control group, 105 children (36.9%) were breast-fed for less than 6 months, and 22 children (7.7%) had never been breast-fed. The differences between the two groups were statistically insignificant. The frequency of malnutrition and anemia were higher in the rachitic group than in the control group (Table III).

### Table I. Causes of Admission to Hospital of Rachitic Cases

<table>
<thead>
<tr>
<th>Causes</th>
<th>Number of cases</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory system infections</td>
<td>10</td>
<td>47.6</td>
</tr>
<tr>
<td>Hypocalcemic seizure</td>
<td>6</td>
<td>28.5</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>2</td>
<td>9.5</td>
</tr>
<tr>
<td>Findings of urinary system infection</td>
<td>1</td>
<td>4.7</td>
</tr>
<tr>
<td>Fever</td>
<td>1</td>
<td>4.7</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>1</td>
<td>4.7</td>
</tr>
</tbody>
</table>

### Table II. Biochemical Results of Rachitic Cases According to Stages

<table>
<thead>
<tr>
<th>Stages</th>
<th>Calcium (mg/dl)</th>
<th>Phosphorus (mg/dl)</th>
<th>ALP (IU/L)</th>
<th>Vitamin D level (µg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>7.71 ± 1.26</td>
<td>6.08 ± 0.94</td>
<td>277 ± 169.2</td>
<td>9.4 ± 2.1</td>
</tr>
<tr>
<td>Stage II</td>
<td>8.62 ± 0.75</td>
<td>3.75 ± 1.49</td>
<td>539.5 ± 458.9</td>
<td>8.7 ± 5.3</td>
</tr>
<tr>
<td>Stage III</td>
<td>6.02 ± 1.12</td>
<td>4.12 ± 1.67</td>
<td>688.2 ± 325.7</td>
<td>8.1 ± 4.6</td>
</tr>
<tr>
<td>Total</td>
<td>7.41 ± 1.54</td>
<td>4.98 ± 1.65</td>
<td>462 ± 335</td>
<td>8.3 ± 4.1</td>
</tr>
</tbody>
</table>

ALP: Alkaline phosphatase.

### Table III. Comparison of Rachitic Cases with Non-Rachitic Cases

<table>
<thead>
<tr>
<th></th>
<th>Rachitic cases (n: 21)</th>
<th>Non-rachitic patients (n: 284)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Covered mother</td>
<td>17 (80.9%)</td>
<td>163 (57.3%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Anemia</td>
<td>15 (71.4%)</td>
<td>119 (41.9%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Breast feeding for at least 6 months</td>
<td>10 (47.6%)</td>
<td>127 (44.7%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>No vitamin D supplementation</td>
<td>16 (76.1%)</td>
<td>101 (35.5%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>7 (33.3%)</td>
<td>16 (5.6%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Low monthly income*</td>
<td>20 (95.2%)</td>
<td>187 (65.8%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Infectious findings on admission</td>
<td>14 (66.6%)</td>
<td>119 (41.9%)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

*According to National Statistics Institute data.
Eleven children in the rachitic group had typical rachitic X-ray findings such as cupping and/or widening of the distal ends of the radius and ulna. X-ray findings of all rachitic patients improved after the 3-week treatment with the exception of 4 patients.

When the mothers of the rachitic patients were questioned regarding their educational status and knowledge about vitamin D supplement, benefits of sunshine, and risk factors for rickets, it was found that 20 mothers (95.2%) had no information on these subjects. Sixteen families of rachitic children had low social status and low income, and 13 cases lived in houses without sufficient exposure to sunshine.

Discussion
Rickets is frequently seen in countries in which malnutrition, undereducation, and socioeconomic status are significant problems or in populations lacking adequate sunlight exposure for traditional reasons. In our study, the frequency of vitamin D deficient rickets among hospitalized children aged from 0 to 3 years was 6.8% in the capital city, which means that rickets is still an important health problem in our country. In our country, the frequency of nutritional rickets has been reported as 1.7% to 19% in different studies conducted with different age groups and in different geographic areas\(^5,6,12-14\). The prevalence of rickets in Ankara among children 0-5 years old was reported to be 4.1%\(^12\). Varying prevalence values for rickets have been reported in different geographic regions of our country (e.g. 19% in suburb areas in Istanbul in 1970, 14.7% in villages, and 6.9% in the Aegean region). Recent reports suggested the prevalence of rickets in the Kayseri region as 3.2% and in Erzurum as 6.1%\(^6,15-17\). Differences in the frequency of rickets may be caused by different climates and geographic areas, dietary habits, access to medical services, education of the families, and the different age groups included in the studies.

The spectrum for the pathogenesis of nutritional rickets consists of vitamin D deficiency, dietary calcium deficiency, and sometimes a combination of these two situations. Low dietary calcium intake also leads to increased catabolism of vitamin D\(^18\). Vitamin D deficiency is the major cause of rickets among young infants in most developing countries like Turkey. In this study, all children with rickets had low vitamin D levels and hypocalcemic children improved after vitamin D and initiation of calcium supplementation. Patient generally have marginal or low vitamin D stores and a diet deficient in calcium and/or high in substances that may impair intestinal absorption of dietary calcium could have been a factor in some of our patients.

In some African countries like Nigeria, despite sufficient sun exposure, rickets occurs because of inadequate intake of calcium\(^19\), while lack of exposure to sunshine is the main problem in North European countries. In the United States, the reemergence of vitamin D deficiency as a public health problem has been recently reported\(^2\).

Anemia and malnutrition are frequently seen in rachitic cases\(^20,21\). In our study, microcytic anemia was present in 71.4% of rachitic cases, and all were iron deficiency anemias. Malnutrition was found in seven rachitic children. It was obvious that the cases were inadequately and insufficiently nourished, which was associated with vitamin D and calcium deficiency. In rachitic cases, nutritional anemia, myelofibrosis and extramedullary hematopoiesis could also worsen the depth of anemia\(^22\).

Rickets could be a predisposing factor for respiratory tract infections\(^5,7\). Pneumonia frequency is found to be five times higher in rachitic cases\(^23\). In our cases, respiratory tract problems were the most common reason for hospitalization. In a study from Jordan, a very high rate (85.1%) of respiratory tract infection in the rachitic children was reported\(^24\). Deformities of the thorax, compression of the lung tissue, hypocalcemic myopathy of intercostal muscles, and changes in humoral and cellular immunity are the suspected mechanisms for pneumonia in rachitic cases. Vitamin D is also an important regulatory vitamin of the immune system\(^25,26\).

Most of our vitamin D deficient children were under one year old. Early occurrence of rickets could depend on various factors. It is known that concentrations of metabolites related to bone health in breast milk and cow’s milk are far from meeting the requirements in the infancy period\(^6,27\). The vitamin D level of the newborn reflects their mother’s
level. Insufficient vitamin D stores and/or low vitamin D intake of the mother during pregnancy lead to congenital rickets and neonatal tetanies of the infant. Infants born with low vitamin D stores and perpetuated with low additional vitamin D would develop rickets. Andiran et al. found that 80% of healthy breast-fed newborns had low serum 25(OH)D$_3$ level, and 48% of their mothers had low 25(OH)D$_3$ levels. Low maternal serum 25(OH)D$_3$ levels were found to be associated with low socioeconomic class, being covered, and low educational level.

These data indicate that the solution to rickets requires specific attention during pregnancy and the early infancy period. Routine vitamin D supplementation or periodic determination of vitamin D status during pregnancy would be the first step to decrease rickets occurrence during the infancy period. Education about the importance of weaning children to a diet adequate in both vitamin D and calcium should be emphasized. Insufficient maternal vitamin D supplementation during pregnancy, covered mothers, low educational and socioeconomic status, and pregnancies without regular medical visits indicated a severe risk of vitamin D deficiency, and urgent initiation of vitamin D supplementation in children could prevent the development of rickets. The high frequency (33.3%) of cases in stage III in our study points to the severity of vitamin D deficiency in our population and the longer time interval to diagnosis. It was reported that vitamin D deficiency in utero and during the first year of life has devastating consequences and might have an imprint on the child's life for development of chronic diseases. Neonates who are vitamin D deficient during the first year of life have a 2.4-fold risk of developing type 1 diabetes when compared to children who received vitamin D. Muscle function, innate immunity, cellular growth and maturation, immunomodulation, insulin secretion, as well as regulation of calcium/phosphorus and bone metabolism are all affected or controlled by vitamin D.

In conclusion, nutritional rickets is still a common and serious health problem in our country. Monitoring of serum 25(OH)D$_3$ concentration during pregnancy, sufficient maternal supplementation, education of the population, and early vitamin D supplementation during the infancy period, especially in those at high risk (i.e. covered mothers and those with low socioeconomic status), would decrease disorders due to the vitamin D deficiency. Thus, ensuring that women are not lacking in vitamin D during pregnancy and that newborns are either immediately evaluated regarding their vitamin D status by measurement of 25(OH)D$_3$ levels in cord blood or given vitamin D prophylactically should be a high priority in Turkey.

REFERENCES


