ABSTRACT

Purpose. To evaluate early adolescents with nutritional rickets and their responses to treatment.

Methods. 203 adolescents (aged 10 to 13 years) presenting with clinical features of lower-limb deformity, carpopedal spasm, joint swelling, a significant limp, or non-traumatic joint pain were screened for nutritional rickets. Multi-specialty examinations were performed. Family size, number of earning members, number and gender of children, preference for vegetarian food, composition of the meals, and the amount of milk consumed in a day were recorded. Radiographs of wrists, knees, ankles, and pelvis, as well as serum calcium, phosphate, and alkaline phosphatase levels were evaluated. The diagnosis of nutritional rickets was made based on a combination of clinical, radiological, and biochemical criteria, and confirmed by the responses to treatment. Children with nutritional rickets were treated by a single large intramuscular dose of vitamin D (600 000 IU) along with oral calcium and supplementary vitamin D as well as advice on diet and sunlight exposure.

Results. 40 females and 11 males were diagnosed as having nutritional rickets. 65% presented with bilateral knee pain with aggravation at night, 37% presented with lower-limb deformity, 24% had joint swelling especially at the wrist and ankle, 6% had a significant limp and walked with an antalgic gait secondary to pathological fractures. No patient reported carpo-pedal spasm. All patients had rachitic changes on radiographs in some but not all bones (100% in the ulna, 45% in the radius, 37% in the upper tibia, 37% in the lower fibula and 22% in the lower tibia). Three patients had pathological fractures. 55% had hypocalcaemia, 41% had hypophosphataemia and 100% had raised serum alkaline phosphatase levels. The mean time for biochemical resolution was 12 (range, 3–24) weeks. For radiological resolution it was 5 (range, 2–6) months, with the lower end of ulna being last to resolve.

Conclusions. Radiographs of the lower end of ulna and serum alkaline phosphatase levels can be used as a screening and monitoring tool for nutritional rickets in early adolescents. There may be a high prevalence of subclinical vitamin-D deficiency in our adolescent population.

Key words: adolescent; child; rickets; ulna
INTRODUCTION

Development from early adolescence to puberty involves accelerated growth in a short period of time. The metabolic reserves are under great pressure during this spurt in growth. The increased metabolic demands together with dark skin pigmentation, low vitamin-D intake, and lack of sunlight exposure may predispose this age-group to nutritional rickets.\textsuperscript{1,2} The diagnosis of rickets is difficult as its presentation in adolescents may be subtle and nonspecific.\textsuperscript{1,3,4} Adolescent nutritional rickets in temperate and tropical countries have been reported.\textsuperscript{5} We assessed the various presentations of nutritional rickets in early adolescents and evaluated their responses to treatment.

MATERIALS AND METHODS

The ethics committee of our hospitals approved this study. Informed consent was obtained from each patient’s attendant. Between November 2006 and August 2008, 203 adolescents (aged 10 to 13 years)\textsuperscript{6} presenting with clinical features of lower-limb deformity (genu varum and valgum, defined as intercondylar and intermalleolar distances of >6 cm and >8 cm, respectively),\textsuperscript{7} carpopedal spasm, joint swelling, a significant limp, or non-traumatic joint pain were screened for nutritional rickets. Each child underwent multi-specialty examination (central nervous system, dermatological, urological, gastrointestinal, ophthalmological, musculoskeletal, dental systems). A detailed dietary history was not elicited. Family size, number of earning members, number and gender of children, preference for vegetarian food, composition of meals, and the amount of milk consumed in a day were recorded. Radiographs of wrists, knees, ankles, and pelvis were evaluated. Radiological changes were usually present in the knee and wrist and were classified as diffuse and eccentric increase in physeal height (Table). The serum calcium, phosphate, and alkaline phosphatase levels were estimated. Investigations of Vitamin D and parathyroid hormone levels could not be ascertained because they were not available at our institution.

The diagnosis of nutritional rickets was made based on a combination of clinical (exclusion of other causes), radiological (widening of the physis, metaphyseal strips and in severe cases the typical cupping, splaying and fraying of the metaphysis, as well as decreased metaphyseal bone density),\textsuperscript{2,8} and biochemical (low serum calcium and phosphorus and raised alkaline phosphatase levels) criteria, and confirmed by responses to treatment.

Patients with clinical features suggestive of any concurrent systemic illness, intake of any drug interfering with bone turnover, arthropathies, and any other skeletal disease were excluded. Patients with rickets caused by chronic diarrhea, renal or hepatic disease, malabsorption, epilepsy, and fluorosis were also excluded based on history and clinical examination of various systems, as well as investigation of haematological, urine, stool and imaging results.

Children with nutritional rickets were treated by a single large intramuscular dose of vitamin D (600 000 IU)\textsuperscript{9} along with oral calcium and supplementary vitamin D as well as advice on diet and sunlight exposure. The children were followed up at week 3 to assess the responses to treatment and subsequently at a 6-week interval until radiological and biochemical resolution. The conversion of the lower ulnar metaphyseal margin from concave to convex was taken as evidence of radiological resolution (Fig. 1). The normal laboratory reference values of serum calcium were 9.10 to 11.04 mg/dl, serum phosphorus 2.5 to 4.8 mg/dl, and serum alkaline phosphatase 180 to 640 IU/l.

RESULTS

58 of 203 patients were diagnosed as having rickets; of them 7 were not attributed to malnutrition but to renal disease (n=4), malabsorption syndrome (n=1), or anti-convulsant drugs intake (n=2) and thus excluded. Of the remaining 51 (40 females and 11 males), 33 (65\%) presented with bilateral knee pain with aggravation at night, 19 (37\%) presented with lower-limb deformity (16 bilaterally) such as genu valgum (n=15) and genu

<table>
<thead>
<tr>
<th>Diffuse increase in physeal height</th>
<th>Eccentric increase in physeal height</th>
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<tr>
<td>Younger skeleton</td>
<td>Older and mature skeleton</td>
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<td>More severe</td>
<td>Less severe</td>
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<td>More bones involved</td>
<td>Fewer bones involved</td>
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<tr>
<td>More biochemical derangement</td>
<td>Less biochemical derangement</td>
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<tr>
<td>Predominantly present with joint swelling</td>
<td>Predominantly present with joint deformity and/or pain</td>
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Table

Radiological patterns of nutritional rickets in early adolescents
varum (n=4), 12 (24%) had joint swelling especially at the wrist and ankle, 3 (6%) had a significant limp and walked with an antalgic (pain avoiding) gait secondary to pathological fractures, and no patient reported carpo-pedal spasm.

All 51 patients had rachitic changes (widening of physis, metaphyseal streaks, cupping, splaying, fraying) on radiographs of some but not all bones (100% in the lower end of ulna, 45% in the radius, 37% in the knee, 37% in the fibula, 22% in the tibia, and 10% in the upper end of femur). Three of the 5 patients with rachitic changes in the upper end of the femur had pathological fractures (one with bilateral undisplaced fracture of the femoral neck, one with unilateral fracture of the femoral neck, and one with supracondylar fracture of the femur).

In all 51 patients, the serum calcium levels ranged from 5.56 to 11.2 mg/dl, the mean serum calcium and phosphorus levels were 8.61 and 2.7 mg/dl, respectively. 28 (55%) of the patients had hypocalcaemia, 21 (41%) had hypophosphataemia, and all 51 (100%) had raised serum alkaline phosphatase levels (mean, 2041; range, 804–5707 IU/l).

Two patients were lost to follow-up after the first treatment. The remaining 49 patients all showed dramatic clinical, radiological, and biochemical responses 3 weeks after treatment. Only 4 (8%) patients had hypocalcaemia and 5 (10%) had hypophosphataemia. Of the 49 patients, the mean serum calcium and phosphatase levels increased to 9.4 and 3.1 mg/dl, respectively. 46 (94%) of the 49 patients still had raised serum alkaline phosphatase levels (mean, 1310 IU/l). 17 more patients were lost to follow-up after the second treatment. Of the remaining 32 patients, the mean time to biochemical resolution of all 3 parameters was 12 (range, 3–24) weeks. The mean time to radiological resolution was 5 (range, 2–6) months, with the lower end of ulna being last to resolve. Radiological resolution lagged behind biochemical resolution by about 4 months.

DISCUSSION

Adolescents and young adults are more prone to vitamin-D deficiency because of the greater mineral demands of their growing skeletons.1,10–13 Vitamin-D deficiency in adolescents has been reported in cold or temperate countries,14,15 but a high prevalence has been noted even in countries with adequate sunshine throughout the year.16,17

Most of our patients were raised in families of middle-to-low socioeconomic status. Their parents earned daily wages and had 4 to 5 dependent family members. Their main diet was vegetarian, cereal-based (rice or wheat), which is rich in phytates and oxalates. Consumption of milk and dairy products was very low because of unaffordability. Low calcium intake increases the need for already deficient vitamin D and precipitates rickets.18 Another study in north India also found a high prevalence (10.8%) of nutritional rickets among adolescents aged 10 to 18 years.16 The prevalence was 68 per 100 000 children in Saudi Arabia,3 and 9.4% among adolescents in China.19

A female preponderance in nutritional rickets may be due to discrimination against the female gender in India. High atmospheric pollution in Delhi filtering ultraviolet rays may be another factor.20

Presentation of nutritional rickets in early adolescents is non-specific and differs from that in infants and toddlers. Rickets due to familial disorders is noticeable early in life. It is unusual for children with familial or renal tubular defects to remain undiagnosed in adolescence. The typical features of rickets in young infants (such as craniotabes, bossing of frontal and parietal bones, rachitic rosary, pigeon chest, Harrison sulcus, gross swelling of joints due to widening of epiphysis) are not present when the disease manifests at a latter stage of life. Deformities of long bones occur when the rachitic child starts to bear weight. Manifestations of muscle hypotonia seen in severe rickets in infants such as protuberant abdomen and lumbar lordosis are also absent. In adults, calcium and vitamin deficiency causes osteomalacia. Although the presenting features (bone pains, muscular pains, pathological fractures) may resemble those of early...
adolescent rickets, the radiological presentation of osteomalacia is in the form of bone rarefaction and looser’s zones in areas of stress (rather than at the end of long bones).

Limb pain and vague symptoms are the main presenting features of rickets in early adolescents, as is carpopedal spasm. Limb deformities were present in 37% of our cohort, but in other studies the prevalence has ranged from 10 to 12%, and mostly manifested as bilateral genu valgum.

In our study, not all long bone ends demonstrated the typical changes of nutritional rickets. Younger and more severe patients presented with a diffuse increase in the physeal height at long bone ends (Fig. 2), which is a more common pattern. More mature children and milder cases usually presented with an eccentric increase in the physeal height (Fig. 3).

Both patterns were not symmetrical, even for one particular bone, and varied from bone to bone. This may be attributable to differential muscular forces at the ends of various long bones.

Radiographs of the lower end of ulna had high sensitivity and can be used as a screening tool for diagnosing nutritional rickets in early adolescents, as all our patients showed widening of the physis at
this site. Radiological resolution lagged considerably behind biochemical healing. The lower end of ulna was last to resolve. Radiographs can also be used for monitoring the course of treatment. 17 of our patients had fused epiphysis at the knee joint and hence radiological changes in the knee that depicted nutritional rickets could not be commented upon except for osteopenia and a low cortico-medullary ratio. The fusion of the lower femoral epiphysis and upper tibial epiphysis in Indian females can occur at as early as age 14 years and is about 2 to 3 years earlier than in Europeans.22

Pathological fractures are not common in this age-group unless the deficiency is very severe. They have not been reported in other studies2,3,23 except one (reporting 7%). 21

High rates of hypocalcaemia have been reported.2,4 In one study, 90% of 21 adolescents had hypocalcaemia; 12 of whom had carpopedal spasm.3 Nonetheless, a normal mean serum calcium level was reported in another series of 42 adolescents.21 All our patients had raised alkaline phosphatase levels (mean, 2041 IU/l), which was more than 3 times the normal (180–640 IU/l), and was consistent with findings from other studies.3,4,21

A limitation of the study was that we did not enrol controls so as to properly assess treatment response. There were many uncontrollable factors influencing the severity and course of nutritional rickets, namely diet, sunlight exposure, clothing, and stores of vitamin D and calcium in body. The study was conducted in a tertiary care centre, and hence an exact catchment area could not be defined. Thus, our cohort may not represent the true picture of rickets in the region. It does, however, point toward a clinically significant prevalence of subclinical rickets in our locality. All our patients had raised serum alkaline phosphate levels and radiographic changes in the distal ulnar physis. Although the sensitivity of these 2 features was 100%, their specificity and positive and negative predictive values cannot be commented owing to the absence of a control group and considerable overlapping of these features between patients with nutritional and non-nutritional rickets.

CONCLUSION

There may be a high prevalence of subclinical vitamin-D deficiency in our adolescent population. Dietary causes must be kept in mind when dealing with lower limb deformities and knee/leg pains in early adolescents, especially in regions where the prevalence of rickets is high. The American Academy of Pediatrics suggests that all infants, children, and adolescents should have an intake of 400 IU units of vitamin D daily.24 Radiographs of the lower end of ulna and serum alkaline phosphate levels can be used as a screening and monitoring tool for nutritional rickets.

REFERENCES