

Original Articles

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Aetiology and clinical profile of osteomalacia in adolescent girls in northern India:

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ABSTRACT

Background. The adolescent age group is particularly prone to nutritional rickets/osteomalacia due to an increased demand for nutrients, especially calcium and vitamin D. Osteomalacia presents with non-specific signs and symptoms because of which diagnosis may be delayed. Vitamin D deficiency is unexpected in India, which is a tropical country with abundant sunshine.

Methods. We prospectively studied the clinical presentation, aetiology and social factors contributing to adolescent rickets/osteomalacia in our region.

Results. We saw 21 symptomatic adolescents with osteomalacia during the study period (November 2000-July 2002). All were girls. Only 1 practised purda and 4 belonged to a low socioeconomic class. The mean (SD) duration of illness before correct diagnosis was 2.8 (2.1) years. Bone pains and muscular weakness were universally present. Non-specific complaints (especially limb pains being mistaken for joint involvement) led to a delay in diagnosis with consequent morbidity. All but 1 patient had low serum 25-hydroxyvitamin D levels (<10 ng/ml), with the mean (SD) being 4.9 (2.7) ng/ml. Their mean dietary calcium intake was low [265 (199) mg/day, range 40-810 mg/day]. Restricted outdoor activities (n=19) and the traditional dress code (n=21) were contributory factors, as they led to poor exposure to sunshine.

Conclusion. Nutritional osteomalacia among adolescents is a poorly recognized entity. Even in non-purda practising communities in the tropics, poor exposure to sunshine due to social factors, compounded by low dietary calcium intake, can lead to osteomalacia in adolescents.

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INTRODUCTION

More than a century after the aetiology and prevention of nutritional rickets and osteomalacia were described, these conditions remain prevalent both in developed and developing countries.¹⁻⁶ The reasons include lack of adequate sunshine in temperate regions, skin pigmentation in darker races, and low calcium and vitamin D consumption due to poverty or food fads. Adolescent osteomalacia was first reported among Asian immigrants from India and Pakistan to the UK.⁷⁻⁹ The rapid growth rate during adolescence increases the requirement of vitamin D and calcium. Poor exposure to sunshine due to a temperate climate and/or excessive clothing would be expected to further compound this problem. Recent studies from Finland, northern France, Saudi Arabia and China have again brought into focus the issue of vitamin D deficiency during adolescence.^{1-5,10}

In India, we do not share some of the contributory factors postulated in the above geographical regions, in as much as there is no paucity of sunshine and only a minority practise purda. There are no published data on osteomalacia among adolescents living in India. We present our experience with symptomatic adolescent girls with osteomalacia to highlight the varied presentations of the illness in this age group, the aetiology in our sunny country in a predominantly non-purda practising community and the response to therapy.

SUBJECTS AND METHODS

We prospectively studied all adolescents clinically suspected to have rickets/osteomalacia attending the outpatient services of the Endocrinology Department, Sanjay Gandhi Postgraduate Institute of Medical Sciences and the Department of Physical Medicine and Rehabilitation (Rehabilitation and Artificial Limb Centre), Chatrapati Sahuji Maharaj Medical University (formerly King George's Medical College), Lucknow (latitude 26.8° N), from November 2000 to July 2002. The former is a tertiary care centre attended predominantly by the middle socioeconomic group and the latter serves, in addition, people belonging to the low socio-economic strata.

All adolescents in Tanner stage 2 or more of puberty, with onset of symptoms prior to 18 years of age, were included in the study. All patients with a clinical suspicion of rickets/osteomalacia underwent estimation of serum alkaline phosphatase and X-rays of the pelvis or any other clinically relevant site. The

diagnosis was confirmed by an alkaline phosphatase level >200 IU/L¹¹ and radiological features of osteomalacia. The serum alkaline phosphatase level in normal adults in our assay is 30-90 IU/L. Children with renal, hepatic or generalized skin disease, those with malabsorption, or on anticonvulsant or antitubercular drugs prior to the onset of symptoms, or having a family history suggestive of resistant rickets were excluded. Since early marriage is common in this population, those who were pregnant or had given birth to a child were also excluded.

Clinical details of bone or joint pains, muscular weakness, deformities, seizures, tetany, fractures or gait disturbances were noted and information was obtained, with special reference to dietary history and exposure to sunshine. The anthropometric data are in reference to Indian children of the upper socioeconomic class.¹² Calcium and vitamin D intake was assessed by a 3-day diet recall. Details of sun exposure were obtained by the daily duration of time spent outdoors during the various seasons of the year by a direct questionnaire. It was also confirmed indirectly from the details of school timings, mode of transport, time spent in outdoor games, and outdoor and indoor household activities. The socioeconomic factors evaluated included the educational and occupational details of the parents, per capita income and type of housing. Serum calcium, phosphorus and 25-hydroxyvitamin D [25(OH)D] levels were also estimated. The study was approved by our institutional ethics committee.

Biochemical analysis

Serum calcium, phosphorus and alkaline phosphatase levels were measured by commercial kits (Boehringer Mannheim, Mannheim, Germany) using a spectrophotometer. Serum 25(OH)D level was measured by radioimmunoassay kits (Incstar, Minnesota, USA). The limit of detectability for 25(OH)D was 1.5 ng/ml and the interassay variation in our laboratory was 17% at a 25(OH)D level of 15.1 ng/ml.

Treatment and follow up

All the subjects received a single oral dose of 600 000 U of vitamin D and were advised adequate sun exposure. Elemental calcium (as calcium carbonate) was given at a dose of 1 g daily, in three divided doses for 12 months. Patients with multiple pseudofractures of the pelvic bones were advised bed rest for 4-6 weeks. The response was assessed at 1, 3 and 6 months from the start of treatment, with repeat X-ray and estimation of alkaline phosphatase levels at 3-monthly intervals until healing.

RESULTS

Demography

Twenty-five adolescents with osteomalacia presented during the study period. Four were excluded from analysis as they had received antitubercular therapy or irregular treatment with vitamin D previously, rendering their biochemistry uninterpretable. All were girls in whom the mean age at onset of symptoms was 13.6 years (range 9-16.5 years). The mean duration of symptoms was 2.8 years (0.5-6 years). All were of urban origin. Only 4 girls were from a low socioeconomic background; their parents were either illiterate or had received only primary education and there was evidence of overcrowding in the home. The majority belonged to the middle socioeconomic class and their parents were either professionals or businessmen. About 33% belonged to the Muslim community.

| Symptoms at presentation | n |
|--------------------------|----|
| Bone pains | 21 |
| Muscular weakness | 21 |
| Joint pains | 6 |
| Deformity | 5 |
| Tetany | 2 |
| Seizure | 1 |
| Fracture* | 1 |

* 2 of the 4 patients who were excluded from the study because of previous antitubercular therapy also

had a recent history of fracture

Clinical features

The clinical features are shown in Table I. Bone pain was the most striking and distressing complaint. In 7 of them (33%), the pain was excruciating, forcing them to restrict their daily activities and discontinue schooling. In 6 patients, bone pain was mistakenly attributed to joint pains resulting in unnecessary investigations to uncover tuberculosis or a rheumatological disorder. Two girls were referred to a cardiologist with a diagnosis of rheumatic fever before osteomalacia was suspected, and were on prophylaxis for rheumatic fever. Two patients had received antitubercular treatment.

Muscular weakness was the next most prominent symptom and was universally present. A minority (n=2) also complained of a waddling gait. In 2 cases, predominant proximal muscle weakness led to a suspicion of a primary neuromuscular disorder and these patients were referred to the neurologist by their primary physician. The combination of bone pains and muscular weakness with elevated parathormone resulted in the referral diagnosis of primary hyperparathyroidism in 3 girls. Deformities seen in 5 girls included genu valgum, genu varum and coxa vara. Acute manifestations such as seizures and tetany were infrequently seen, probably due to the patients being in the stage when secondary hyperparathyroidism corrects the hypocalcaemia. The mean height standard deviation score was significantly lower than that for the reference population, though weight standard deviation scores were comparable. None of the patients had clinical evidence of other nutritional deficiencies.

Dietary calcium and sun exposure

The mean daily calcium intake was 265 (199) mg (recommended dietary allowance 1200-1500 mg/day in adolescents).¹³ In 17 of them it was stated to be due to personal preferences (distaste for milk) rather than to economic reasons.

The mean exposure to sunlight was 5 (9) and 88 (103) minutes, respectively, in summer and winter. None of the girls had participated in outdoor games even at school, prior to their illness. Their only exposure to the sun was on their way to and from school. There was an even distribution of cases throughout the year. Sun exposure was longer in winters due to a propensity for people to sit in direct sunlight during this season. None of the girls used sunscreens. Only one girl used purda. Even among the Hindus, only the head, neck, forearm and hands were uncovered.

Table II. Baseline clinical and biochemical features of 21 patients with adolescent osteomalacia

| Characteristic | Mean (SD) | Range |
|--|----------------|-------------|
| Age at presentation (years) | 16.2 (2.5) | 13-20 |
| Age at onset of symptoms (years) | 13.6 (1.6) | 9-16.5 |
| Religion (Hindu/Muslim) (n) | 15/6 | |
| Height SDS* | -1.94 (1.36) | |
| Weight SDS* | -0.59 (1.52) | |
| Sun exposure† (min/day) | | |
| summer/winter | 5 (9)/ 88(103) | 0-30/10-360 |
| Calcium intake (mg/day) | 265 (199) | 40-810 |
| Serum alkaline phosphatase (IU/L) (adult normal 30-90 IU/L) | 756 (610) | |
| Serum calcium (mg/dl) (normal 8.5-10 mg/dl) | 8.3 (0.9) | |
| Serum phosphorus (mg/dl) | 2.8 (1.3) | |

| | | |
|---|-----------|------------|
| (normal 3.5-5 mg/dl) | | |
| 25-hydroxyvitamin D (ng/ml) (normal >10 ng/ml) | 4.9 (2.7) | 1.38-10.05 |
| * Standard deviation scores (SDS) with reference to Indian children of higher socioeconomic class ¹² † Area exposed included head, forearm, hands and feet in summer, and only head and hands in winter | | |

Biochemical parameters

All but 1 patient had vitamin D deficiency with a mean 25(OH)D of 4.9 (2.7) ng/ml. The mean 25(OH)D levels in the 14 ambulatory patients was 5.9 (2.6) ng/ml, higher than the 7 non-ambulatory patients [3.4 (2.4) ng/ml] and the difference was significant ($p=0.04$). Nevertheless, both values were below normal (<10 ng/ml) (Table II).

Radiological features

Looser zones (pseudofractures) were seen at the upper end of long bones, and/or pubic or ischial rami ($n=10$) (Fig. 1). Another common finding was a wide and irregular pubic symphysis ($n=12$), which became normal on follow up. Brown tumour was seen in 1 patient who presented with a fracture through the cyst, with delayed union (Fig. 2). A triradiate pelvis was seen in 2 patients.

Response to therapy

All the patients showed clinical improvement on oral vitamin D and calcium supplementation at 1 month of follow up. Proximal myopathy and bone pain improved and all were ambulatory at 1 month. Radiological healing was complete by 3-6 months and the alkaline phosphatase levels became normal between 1 and 9 months (Table III).

| Duration of therapy | Mean SAP (range)* | n | Healed (n) |
|---|-------------------|----|------------|
| 0 | 756 (205-2400) | 21 | 0 |
| 1 | 530 (220-950) | 18 | 3 |
| 3 | 354 (213-769) | 14 | 7 |
| 5 | 286 (205-400) | 5 | 16 |
| * SAP levels of patients with values outside the normal range | | | |

DISCUSSION

Our study highlights the high index of suspicion necessary to make an early diagnosis of osteomalacia in the absence of rickety deformities. Misdiagnosis as arthritis, myopathy or psycho-

somatic illness in these young girls resulted in a delay in diagnosis with associated severe morbidity. As the institutions from which the patients were drawn were referral in nature, mildly affected patients from the community must have been missed. Our study also highlights the socioeconomic reasons that preclude many Indians, particularly girls, from taking advantage of the abundant sunshine available. Adolescent girls are discouraged from outdoor activities (in comparison to boys), so that even non-purda practising girls, who would otherwise be able to expose the face, neck, forearms, arms and hands to sunshine, suffer from severe vitamin D deficiency rickets/osteomalacia. This gender bias is witnessed by the fact that during the period of the study, we did not encounter a single male adolescent patient. The preponderance of girls has been commented on in other reports on adolescent rickets/osteomalacia from tropical middle eastern countries⁴⁻⁶ but not in reports from temperate western countries.^{1,3} El-Haji Fuleihan et al.⁶ observed in a multivariate analysis of Lebanese school-children 10-16 years of age that female gender predicted a low 25(OH)D level, independent of the socioeconomic status and season.

However, these studies were carried out in communities observing purda.

In our study, a low level of 25(OH)D was universal in the adolescent girls with osteomalacia. The cutaneous synthesis of vitamin D depends on the age, melanin pigmentation and the angle of incidence of the sun's rays (which in turn depends on the latitude and season). Thus, synthesis is most efficient under the overhead sun, in the summer season, in less pigmented races and in young people. In our subjects, who were considerably more pigmented than Caucasians, sun exposure was probably inadequate during the summer season. As regards winter, Webb et al.¹⁴ have demonstrated cutaneous vitamin D production to continue throughout the year at Los Angeles (latitude 34° N), though with a lower efficiency in winter. In our subjects, however, though the duration of exposure in winter was greater, the surface area exposed was less than that in summer. It is also pertinent to mention here that studies on the intensity of ultraviolet-B rays reaching the earth's surface in winter in Lucknow showed that the intensity was half that in summer (0.42 v. 0.82 mW/cm², respectively).¹⁵ Our study could not address the issue of seasonal changes in serum vitamin D levels. Goswami et al.¹⁶ reported significantly lower vitamin D levels in winter than in summer in a group of 19 physicians and nurses in New Delhi (latitude 28° N).

Low dietary calcium intake was also a pertinent factor in almost all our patients. Dietary calcium deficiency has been shown to cause secondary vitamin D deficiency.¹⁷ This relationship has also been noted in a study of 1248 Chinese adolescents in whom low dietary calcium predicted the development of subclinical hypovitaminosis D.¹⁰ The authors concluded that it was the low dietary calcium intake of rural subjects that kept their serum vitamin D levels low in spite of better sun exposure as compared to urban subjects. It is worth noting that except in 4 girls in our study, it was not economic considerations but dislike for milk that led to low calcium intake. Moncrieff et al.⁷ also noted this to be a pertinent fact among immigrant Asians in the UK. At the same time, however, we must point out that estimation of calcium intake by a 7-day recall or weighing food items during home visits and during various seasons of the year would have been a better method than a 3-day recall, which is a limitation of our study.

Adolescence is a period of life particularly prone to vitamin D deficiency, as are infancy and pregnancy. Low dietary calcium intake may precipitate clinically significant hypovitaminosis D in these vulnerable groups, in the presence of marginal sun exposure. Investigators in temperate regions such as northern France and Finland have recommended vitamin D supplementation during winter for adolescents.^{2,18,19} Investigators working in tropical and near-tropical latitudes (Saudi Arabia, Lebanon, Beijing) have also made similar recommendations, as the prevalent sociocultural factors cannot be easily changed.^{5,6,10}

In conclusion, adolescents with osteomalacia present with non-specific symptoms, and early recognition requires a high index of suspicion. The importance of public health measures to stress the benefits of adequate sun exposure and dietary calcium intake cannot be overemphasized. This would not only prevent pubertal osteomalacia, but would safeguard against future osteoporosis and complicated pregnancies as a consequence of pelvic deformity, as well as neonatal hypocalcaemia and infantile rickets.

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