VITAMIN D AND ENDEMIC FLUOROSIS

We read with interest the article "Association of vitamin D deficiency with endemic fluorosis in India" by Mishra et al published in the Journal (1). The authors' conclusion that vitamin D deficiency in endemic fluorosis occurs due to lack of dietary vitamin is not supported adequately by their own data or that of others. The major source of vitamin D is sun exposure (2). This is even more true of inhabitants of rural India, the majority of whom are manual labourers exposed to the tropical sun throughout the year. Their diet is cereal based, a poor source of vitamin D. There is poor intake of milk and dairy products. Food products fortified with vitamin D are not available in rural areas. Vitamin D nutritional status of these subjects can not be accurately assessed from calculations based on diet. The accepted method of assessing vitamin D nutrition in any individual is by estimation of serum 25(OH) vitamin D level (2). Serum 25(OH) vitamin D has been reported to be normal in Indian subjects suffering from fluorosis (3,4), including some with radiological evidence of osteoporosis and growth arrest lines.

The data about diet (protein, calories) is inadequately presented. Does 89% deficiency of vitamin D mean that all the habitants of the village were consuming diets 89% deficient in vitamin D, thereby implying that there was no variation in the diet within the village? A similar statement has been made about calories and protein. Was there any correlation of these dietary factors with clinical, biochemical and radiological spectrum, i.e. did subjects with clinical or radiological evidence of vitamin D deficiency have different vitamin D intakes from the others? In the absence of this information it seems difficult to accept the conclusion that dietary vitamin D could have played a major role in determining disease manifestations in the subjects studied.

There is no mention of dietary calcium intake in the subjects studied. Poor calcium intake is rampant in such populations because of low consumption of dairy products. Several reports of rachitogenic effects of low calcium intake are available in literature (5). Calcium deficiency (daily intake less than 150 mg) has been found the causative factor in the pathogenesis of clinically and radiologically proven rickets in Nigerian children. The serum 25(OH) vitamin D and 1,25 (OH)2 vitamin D levels in rachitic children were not significantly different from those in controls but the ratio of 1,25(OH)2 vitamin D to 25(OH) vitamin D was significantly higher than that in controls. Evidence of osteomalacia was present on bone biopsy. Treatment of these children with calcium gluconate (1 gm/d) led to clinical, radiological and biochemical healing of rickets (6). It has been shown in rats that the rate of inactivation of vitamin D in liver is increased by calcium deprivation. The effect is mediated by 1,25 (OH)2 vitamin D produced in response to secondary hyperparathyroidism, which promotes hepatic conversion of vitamin D to polar inactivation products (7).

Furthermore, poor calcium intake has been shown to have a modifying effect on the clinical presentation and radiological pattern of skeletal fluorosis (8,9).

High phytate content in unleavened bread (chupatty) may contribute to development of late rickets and osteomalacia in Asian population (10). Chupatty is the staple diet in North India. Substitution of chupatty with leavened bread of lower extraction in these subjects led to healing of rickets. Sodium phytate enhances the hepatic conversion of 25(OH) vitamin D, an effect which is similar to calcium deprivation (7). Thus the implication of dietary calcium in study of rickets and osteomalacia is particularly important in North India where the diet is primarily cereal based with low intake of dairy products.
It has not been mentioned in what percentage of subjects, children and adults, serum alkaline phosphatase levels were high. Fluoride intoxication or calcium deprivation alone in absence of subnormal 25 (OH) vitamin D levels can lead to elevation of serum alkaline phosphatase (4,6). In two of the water samples analysed, the fluoride content has been reported to be normal. It would be of interest to know whether subjects consuming water with normal fluoride had manifestations of skeletal fluorosis, as has been reported from other countries (11).

We feel that the conclusions the authors have derived from their data are not justified. A typical example of how such information may be misleading to the public is evident from the enclosed newspaper write up (12).

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References

REPLY TO MITHAL AND GODBOLE

Drs Mithal and Godbole suggest the possible role of dietary calcium deficiency in producing rickets and osteomalacia in endemic fluorosis instead of vitamin D deficiency as reported by us. Low dietary calcium leading to rickets is a rare condition. Only a few reports are available and those only in children. It is associated with severe calcium deprivation, dietary intake ranging from 180-150 mg/day (1,2) but such changes have not yet been reported in adults (1-3). In the study from Unnao, rickets and osteomalacia were found in 3 out of 70 patients. Calcium intake of this group was 284±46 mg/day (4). In our study 4 out of 21 adults also had radiological changes suggestive of osteomalacia. Are they implicating the role of dietary calcium deficiency in adults leading to osteomalacia? Daily calcium requirement has been difficult to define (5). Selective deficiency of calcium in human diet is virtually unknown to produce osteomalacia (6). No clear cut disease has been documented even under the condition of low intake as low as 300 mg/day (7). If vitamin D intake is satisfactory osteomalacia and rickets are unlikely with moderate calcium deficiency because of compensatory mechanisms.

In our study we did look at daily calcium and phosphorus intake of 10 families. The average intake was 450 mg and 1000 mg respectively. The radiological changes of rickets and osteomalacia were attributed to vitamin D deficiency which is common in rural areas of the state of Uttar Pradesh. In our subjects serum calcium level was low in 20%, phosphorus was low in 10.5%, alkaline phosphatase was high in 80% of adults and all the children. No doubt serum vitamin D level estimation would have been the ideal method for confirming the deficiency but in its absence dietary analysis with all its limitations was the only way to investigate this problem. The clinical picture, dietary history, radiological features and the commonness of the condition all favoured the possibility of vitamin D deficiency rickets and osteomalacia in our patients.

It seems that the method of dietary analysis has not been understood. The questionary method recommended by the expert group of ICMR was used. Different members of the family were converted into average man coefficient. The nutritive value of all the food items consumed by the family was calculated on the basis of average man coefficient. The results have been compiled into average family requirements of nutrients, actual consumption of nutrients and the difference thereof. Individual correlation of nutritional status with the radiological changes thus was not possible.

Normal serum 25 OH D levels in two Indian studies on fluorosis have been quoted (8,9) and their results have been used to exclude vitamin D deficiency in endemic fluorosis. Both these studies were aimed at studying the endocrinal changes in fluorosis and the subjects in these studies were not reported to be having significant nutritional deficiency. However, in the study of Srivasta et al, one out of five patients did have severe protein and caloric deficiency, low serum calcium and subnormal levels of 25 OH D and 1, 25 (OH) D concentration highlighting the presence of vitamin D deficiency in endemic fluorosis patients (9). Lack of low serum 25 OH D and 1, 25 (OH) D levels in the patients with growth arrest lines in radiographs does not exclude the possible role of vitamin D deficiency. Growth arrest lines indicate nutritional or metabolic abnormality interfering with bone growth at the specific time. They persist even after the deficiency has been made up and hence they may not correlate with present vitamin D level or other parameters of nutritional status. It is surprising that the authors consider dietary calcium deficiency as a cause of osteomalacia and rickets though the dietary calcium intake in their patients was 284±46 mg/day which does not seem to be low enough to produce rickets or osteo-
malacia based on the information currently available (1-3). They presume that vitamin D level in their subjects was normal though neither its serum level nor the dietary intake was estimated (3). Vitamin D deficiency is the commonest cause of nutritional rickets and osteomalacia as mentioned in standard medical texts (10).

Fluorosis produces complex changes in the bone which are because of secondary calcium deficiency produced by fluorosis itself, endocrinal changes which have been extensively reported and the nutritional aspects which have been highlighted by us. The latter may be especially important in India and other developing countries where fluorosis is endemic. Excluding the role of dietary vitamin D because of tropical sunshine, and extrapolating the rare reports of calcium deficiency rickets to the problem of nutritional rickets, and even osteomalacia which is presently regarded to be due to vitamin D deficiency, may be misleading. The suggestion of primary role of dietary calcium deficiency in rickets and osteomalacia should await more scientific evidence.

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References