

## Editorial

### Nutrition & bone health

Nutrition and bone health is tale of two nutrients: calcium and vitamin D. Studies carried out in the last century brought to light several complex and intricate interactions between these two seemingly simple nutrients and bone with several twists and turns. The new century has brought answers to some questions but raised many more issues. The Nutrition Foundation of India (NFI) and Centre for Research in Nutrition Support Systems (CRNSS) organized a two day Symposium on “Nutrition and Bone Health” on 31<sup>st</sup> July and 1<sup>st</sup> August 2007 in Delhi to discuss physiology and molecular biology of vitamin D and calcium, prevalence of calcium and vitamin D deficiencies in different ages and physiological groups, clinical consequences of vitamin D deficiency in infancy and childhood, prevalence of nutrition related bone diseases in various age groups in India and abroad. This is perhaps the right time to assess the current knowledge regarding vitamin D and calcium in bone health and disease, to assess appropriate public health policies to improve bone health, and to identify future research priorities in nutrition and bone health. Some papers from the meet are published in this issue of the IJMR.

#### Calcium and vitamin D requirements

*Calcium:* Calcium requirements are determined from calcium balance studies in healthy adults. In adults, the rate of calcium absorption from the gastrointestinal tract should match the rate of losses from the body. Positive calcium balance (*i.e.*, net calcium retention) is required in pregnant women for growth of the foetus, in children especially during the first two years and during adolescent growth spurt. Postmenopausal women and elderly men require higher calcium intake to maintain bone health.

There are very wide variations in calcium intake between countries depending largely on dairy product

consumption. In developing countries calcium intakes are low (average of 344 mg), as compared to developed countries (average of 850 mg). The huge variations in calcium intakes across the countries of the world do not appear to be associated with commensurate variations in the prevalence of osteoporosis. FAO/WHO Expert Consultation<sup>1</sup> stated that the possibility that calcium requirement may itself vary depending upon dietary, genetic, lifestyle, and geographical factors should be explored. This Consultation<sup>1</sup> recommended calcium requirements based on data from developed countries (notably Norway and the United States) with the proviso that these recommendations can only be applied to countries and populations with similar dietary cultures; other dietary cultures may entail different calcium requirements and call for different recommendations<sup>1</sup>. Thus calcium has the distinction of being the first nutrient for which FAO/WHO Expert Consultation made a recommendation that requirements for nutrients should take into account realities of regional disparities in dietary intakes.

*Vitamin D:* Vitamin D is unique because it is a vitamin synthesized by the body and it functions as a hormone. Vitamin D modulates the transcription of cell cycle proteins, which decrease cell proliferation and increase cell differentiation of a number of specialized cells of the body (osteoclastic precursors, enterocytes, keratinocytes). This property may explain the actions of vitamin D in bone resorption and intestinal calcium transport. Vitamin D also possesses immunomodulatory properties that may alter responses to infections *in vivo*. These properties may explain the reported associations between vitamin D deficiency on one hand and metabolic diseases such as type 2 diabetes, autoimmune diseases, infections such as tuberculosis and some malignancies on the other.

The FAO/WHO Expert Consultation<sup>1</sup> stated that in most locations in the world in a broad band around the equator (between latitudes 42°N and 42°S), the most physiologically relevant and efficient way of acquiring vitamin D is to synthesize it endogenously in the skin from 7-dehydrocholesterol by 30 min of skin exposure (without sunscreen) of the arms and face to sun. Skin synthesis of vitamin D is negatively influenced by factors such as latitude and season; the ageing process; skin pigmentation; clothing and sunscreen use.

### **Vitamin D status in pregnancy**

Osteomalacia in *purdha* wearing north Indian women was a well recognized clinical entity<sup>2</sup>. However, by mid twentieth century it looked as if osteomalacia in women, and babies with congenital rickets was no longer a clinical problem and interest in vitamin D status in pregnant women waned. Neonatal hypocalcaemia among Asian immigrants in UK was attributed to poor maternal exposure to sun light among the immigrants. Vitamin D supplementation during pregnancy to the at risk Asian mothers in UK was suggested as the remedy<sup>3</sup>. As obstetricians in India did not see osteomalacia and paediatricians did not report hypocalcaemia in neonates, it was assumed that Indians in India did not face these problems. With the availability of 25(OH)D assays it has been possible to undertake studies of vitamin D levels and assess prevalence of asymptomatic vitamin D deficiency in population groups. The cut-off levels suggested are as follows: deficiency: serum 25(OH)D < 20 ng/ml; insufficiency: serum 25(OH)D = 20 to 30 ng/ml; and sufficiency: serum 25(OH)D >30 ng/ml<sup>4</sup>.

It is important to build up epidemiological data on vitamin D status of women in different parts of the country and the long term implications of low vitamin D levels and low dietary intake of calcium intake on the peak bone mass and bone mineral density in women. In view of the high prevalence of biochemical vitamin D deficiency, low calcium intake, and known adverse consequences of poor vitamin D status on the mother child dyad, calcium and vitamin D supplementation during pregnancy had been advocated<sup>5</sup>. It is essential to undertake studies to find out dosage and benefits of calcium and vitamin D supplementation during pregnancy before embarking on a massive supplementation programme.

### **Neonatal hypocalcaemia and rickets**

Vitamin D content of breast milk is low and infants do not get adequate exposure to sunlight. Breast fed

infants in developing countries are at risk of developing vitamin D deficiency, if vitamin D stores acquired *in utero* are too low to support infant's high rate of skeletal growth. In developed countries majority of the infants are formula fed. Infant formulas are fortified with vitamin D at levels (40-100 international units) sufficient to prevent rickets. Consequently, vitamin D deficiency in infancy is rare in developed countries.

During the last two decades there have been increased reports of neonatal hypocalcaemia and rickets from different parts of the world<sup>6</sup>. Resurgence of rickets in Europe and USA have been attributed to an increase in the prevalence of breast-feeding, increasing use of sunscreen lotions by Caucasian women in these countries, and dark skinned immigrants not getting adequate exposure to sun light.

Although there are very few epidemiological studies, there is an impression that vitamin D deficiency as defined by low circulating 25(OH)D concentrations is common during infancy and childhood. There are substantial differences in the latitudes and exposure to sunlight between south and north India. Epidemiological studies to assess prevalence of vitamin D deficiency in infancy and childhood in different parts of the country have to be taken up to assess whether prevalence of vitamin D deficiency is higher in northern India. There are increasing number of reports from India on neonatal hypocalcaemia, hypocalcaemic symptoms in young infants<sup>7</sup>, vitamin D deficiency in breastfed infants and clinical and radiological rickets children of all ages<sup>8,9</sup>. Vitamin D deficiency is thought to be the major factor responsible for rickets in India.

Studies on rickets in Nigeria<sup>6</sup> have shown that there is no difference in calcium intakes between controls and affected children, but low dietary calcium intakes have been thought to play a role in the pathogenesis of rickets. In South Africa nutritional rickets is caused by either vitamin D or dietary calcium deficiency; in majority of children with rickets, both coexist. Studies in South Africa<sup>6</sup> suggest that in presence of low dietary calcium intakes, vitamin D requirements may be higher than normal, predisposing those children with low normal range vitamin D levels to rickets. If this is so, the currently accepted normal range for vitamin D sufficiency would need to be adjusted depending on dietary calcium intakes.

### Calcium, vitamin D status and bone mineral density

Data on vitamin D levels, calcium intakes and bone mineral density (BMD) in urban and rural populations belonging to different age and socio-economic groups from India are required in view of their varying calcium intakes and exposure to sunlight. Studies in Delhi school children reported in this issue<sup>9</sup> had shown that about 10 per cent of apparently normal school children had clinical evidence of vitamin D deficiency and a third had 25(OH)D levels below 9 ng/ml. Prevalence of vitamin D deficiency was higher in girls and lower income group children. The mean BMD was significantly higher in high income group children. Age, height and weight explained approximately 50 per cent of the variability, while biochemical parameters explained 30 per cent of variability in BMD. Ongoing studies indicate that the BMD and peak bone mass in Indian women are lower as compared to Caucasians<sup>10</sup>. The relative roles of nutritional status and stature, vitamin D and calcium status as determinants of the low BMD in Indians requires further explorations.

Adequate exposure to sunlight can provide sufficient vitamin D to children and adults. It is therefore imperative that nutrition and health education to improve exposure to sun gets due attention. These efforts will also result in increase in physical activity (play in schools and walks for adults) which will reduce risk of overnutrition and associated risk of non communicable diseases and improve muscle and bone health.

Prevalence of stunting is high in Indian children from low income group. Low birth weight, poor infant and young child feeding, problems in shifting to adult food with low energy density have been thought to be the major factors responsible for high undernutrition and stunting rates in Indian children<sup>11</sup>. It is well known that dietary calcium intake in children is low. Data from studies presented in this issue show that vitamin D status of children is also poor<sup>12</sup>. It may be worthwhile to study the impact of calcium and vitamin D supplementation in young children on stunting rates.

### Osteopaenia and osteoporotic fractures

Osteoporosis and osteoporotic fractures in the elderly especially in postmenopausal women have long been recognised as a major problem. Studies on vitamin D have suggested that there is an age-related decline in many key steps of vitamin D action including the rate

of skin synthesis, the rate of hydroxylation (leading to the activation to the hormonal form), and the response of target tissues (*e.g.*, bone). A number of studies have shown that vitamin D deficiency characterized by low blood levels of 25(OH)D coupled with elevations in plasma parathyroid hormone and alkaline phosphatase is seen in a subset of the elderly population at higher risk of declining bone mass and increased the incidence of osteoporotic fractures.

Studies from developed countries have shown that vitamin D and calcium supplementation, can reduce the rate of bone loss and the incidence of hip fractures by 15 -50 per cent in postmenopausal women and elderly men<sup>13</sup>. Many physicians in these countries recommend routine supplements of calcium 1000 mg/day and vitamin D 800 units/day in women beyond fifty years of age to reduce risk of fracture. Orthopaedic surgeons in India have been concerned at the reported low BMD, peak bone mass and high prevalence of osteopaenia in Indians especially women<sup>14</sup>. An estimated 25 million Indians may have osteopaenia. Osteoporotic fractures in India have been reported to occur in both sexes, at a younger age than in the west. In view of the increasing longevity, there is an urgent need to undertake epidemiological studies to obtain data on osteoporosis and fracture risk. Simultaneously studies to assess the dose needed and effect of prophylactic calcium and vitamin D supplementation in those in their fifties and those over sixty on reducing the risk of fracture have to be taken up.

### Way forward

The importance of adequate calcium intake and vitamin D levels for optimal bone health is well known. There is consensus that adequate sun exposure can provide sufficient vitamin D to humans. Well-designed epidemiological studies have to be taken up to provide the answer to the question "what is adequate area and duration of exposure"? There is no danger of hypervitaminosis following extensive exposure to sun. In view of this, the public health recommendation should be to increase exposure to sun at all ages and in both sexes. Traditional practices such as massaging the infant in the sun should be supported. Outdoor games in schools at least for 45 min, daily walk in sun for 45 min for adults should become a way of life. Such a lifestyle change will also bring in the benefits of increased physical activity such as reduction in overnutrition rates and risk of non communicable diseases.

In view of the reported high prevalence of asymptomatic vitamin D deficiency in Indians, it is essential to initiate epidemiological studies to determine circulating 25(OH)D levels in pregnant women, infants, children of all ages, adult men and women and the elderly living in different parts of the country, in different seasons. Clinical studies on dose of oral vitamin D needed to maintain normal 25(OH)D concentrations in apparently normal persons and some high risk groups such as pregnant women should also be taken up.

The Calcium requirements and how they can be met is a more difficult issue as calcium intake in Indians is low. Calcium balance studies in Indians on habitual low calcium intake need to be taken up to arrive at recommendations on calcium requirements. Studies on effect of varying dietary calcium intakes and vitamin D levels on BMD and peak bone mass should be taken up. Studies on criteria for diagnosis of osteopaenia, osteoporosis in Indians and epidemiology of fractures in the elderly in relation to bone density measurements and osteoporosis are urgently needed. Studies to assess the need for supplementation of calcium and vitamin D and the dose for at risk groups such as pregnant women to improve foetal stores, in children to prevent rickets and stunting, in people in their fifties and beyond to prevent osteoporotic fractures are required in order to ensure that evidence based decisions on supplementation are taken.

**Sarath Gopalan & Prema Ramachandran\***

Nutrition Foundation of India  
C-13, Qutab Institutional Area  
New Delhi 110 016, India

\*For correspondence:  
premaramachandran@gmail.com

## References

1. Report of the Joint FAO/WHO Expert Consultation on vitamin and mineral requirement in human nutrition: Bangkok 1998. Second Edition FAO Rome, 2004. Available at <http://whqlibdoc.who.int/publications/2004/9241546123.pdf>.
2. Teotia M, Teotias PS. Vitamin D deficiency osteomalacia. In: Sainani GS, editor. *API text book of medicine*, 6th ed. Mumbai: Association of Physicians of India; 1999. p. 1086-97.
3. Brooke OG, Brown IR, Bone CD, Carter ND, Cleeve HJ, Maxwell JD, *et al*. Vitamin D supplements in pregnant Asian women: effects on calcium status and fetal growth. *Br Med J* 1980; 280 : 751-4.
4. Hollis BW. Circulating 25 hydroxy D levels indicative of vitamin D insufficiency: implications of reestablishing a new effective dietary intake recommendation for vitamin D. *J Nutr* 2005; 135 : 317-22.
5. Sachan A, Gupta R, Das V, Aggarwal A, Awasthi PK, Bhatia V. High prevalence of vitamin D deficiency among pregnant women and new born in India. *Am J Clin Nutr* 2005; 81 : 1060-4.
6. John M. Pettifor. Vitamin D &/or calcium deficiency rickets in infants and children; a global perspective. *Indian J Med Res* 2008; 127 : 245-9.
7. Balasubramanian S, Ganesh R. Vitamin D deficiency in exclusively breast-fed infants. *Indian J Med Res* 2008; 127 : 250-5.
8. Bhattacharya AK. Nutritional rickets in the tropics. *World Rev Nutr Diet* 1992; 67 : 140-97.
9. Marwah RK, Sripathy Gopalkrishna. Vitamin D & bone mineral density of healthy school children in northern India. *Indian J Med Res* 2008; 127 : 239-44.
10. Shatrugna V, Kulkarni B, Kumar PA, Rani KU, Balakrishna N. Bone status of Indian women from a low-income group and its relationship to the nutritional status. *Osteoporos Int* 2005; 16 : 1827-35.
11. Ramachandran P. Nutrition transition in India and emerging dual nutrition burden in children. *Ann Natl Acad Med Sci* 2007; 43 : 1-24.
12. Chapuy MC, Arlott ME, Duboeuf F, Brun J, Crouzet B, Arnand S, *et al*. Vitamin D3 and calcium to prevent hip fractures in women. *N Engl J Med* 1992; 327 : 1637-42.
13. Malthotra Nidhi, Mithal Ambish. Osteoporosis in Indians. *Indian J Med Res* 2008; 127 : 263-8.