

## Review Article

Indian J Med Res 127, March 2008, pp 250-255

# Vitamin D deficiency in exclusively breast-fed infants

S. Balasubramanian & R. Ganesh

*Kanchi Kamakoti CHILDS Trust Hospital, Chennai, India*

Received October 1, 2007

Exclusive breast-feeding is recommended up to 6 months of age with all its beneficial effects on child survival. Several studies have concluded that adequate intake of vitamin D cannot be met with human milk as the sole source of vitamin D. As breast-feeding rates increase, the incidence of vitamin D deficiency rickets is also expected to rise. One of the potential sources of vitamin D synthesis is in the skin from the ultraviolet rays of sunlight. Risk factors for developing vitamin D deficiency and rickets include low maternal levels of vitamin D, indoor confinement during the day, living at higher altitudes, living in urban areas with tall buildings, air pollution, darker skin pigmentation, use of sunscreen and covering much or all of the body when outside. In a study of 50 cases of hypocalcaemia reported from an urban tertiary care children's hospital in Chennai, 13 exclusively breast-fed infants presented with hypocalcaemia due to vitamin D deficiency and most of them with seizures. None of them had received vitamin D supplementation and all their mothers had biochemical evidence for vitamin D deficiency. This review discusses the rising incidence of vitamin D deficiency in infancy and the need to consider and implement methods to prevent the same by supplementation and increased exposure to sunlight without the hazards of ultraviolet rays on the skin. Further research to define the magnitude of vitamin D deficiency in exclusively breast-fed infants as a public health and paediatric problem and to recommend programmes to prevent the same are of utmost importance.

**Key words** Breast feeding - hypocalcaemia - rickets - vitamin D

### Introduction

Exclusive breast-feeding is recommended up to 6 months of age with all its beneficial effects on child survival. Globally as many as 1.45 million lives are lost due to suboptimal breast-feeding in developing countries. WHO analysis of childhood deaths has listed suboptimal breast-feeding as one of the most powerful shared risk factors and estimated that 1.3 million deaths can be prevented in 42 high mortality countries by increasing the level of breast-feeding amongst infants<sup>1</sup>.

The increase in the practice of breast-feeding, associated with the belief that "breast is best" and that breast milk does not require supplementation because it is a baby's "perfect food," may lead to decreased 25-hydroxy vitamin D(25-OHD) intake from other sources and thereby causing rickets. In this review, we have attempted to discuss the reasons for the increase in vitamin D deficiency in exclusively breast-fed infants and outline the clinical manifestations, management and strategies for prevention of this nutritional disorder.

### Recommended daily allowance of vitamin D

An intake of 200 IU/day of vitamin D has been recommended for normal infants, children and adolescents<sup>2</sup>. The appropriate daily allowance of vitamin D during pregnancy and lactation is unknown, although it appears to be greater than the current dietary reference intake of 200-400 IU/day. However, an earlier published review of vitamin D supplementation during pregnancy concluded that there is not enough evidence to recommend the appropriate requirements and effects of vitamin D supplementation during pregnancy<sup>3</sup>.

### Prevalence and risk factors for deficiency

It has been postulated that the incidence of vitamin D deficiency rickets will increase if breast-feeding rates increase<sup>4</sup>. The prevalence of hypovitaminosis D in exclusively breastfed infants has been reported to be 82, 52 and 20 per cent from UAE<sup>5</sup>, Pakistan<sup>6</sup> and China<sup>7</sup> respectively but there is a paucity of data from India regarding the same. The vitamin D stores of the newborn depend entirely on the vitamin D stores of the mother. Hence, if the mother is vitamin D-deficient, the infant will be deficient because of decreased maternal foetal transfer of vitamin D<sup>8</sup>. There are reports suggesting that the bone mass of the newborn is related to the vitamin D status of the mother<sup>9</sup>. Impaired foetal bone ossification in association with maternal vitamin D deficiency has been reported<sup>10</sup>. The risk factors associated with low maternal 25-OHD include low educational level, insufficient intake of vitamin D in diet and dressing habits<sup>11</sup>. In addition, air pollution may decrease the ultraviolet light exposure and thereby vitamin D production by the skin. In a study from India, enrolling 9-24 month old infants with the same socio-economic conditions and with no vitamin D supplementation, the group living in the region with intensive air pollution had lower serum 25-OHD levels than those living in the region with no air pollution<sup>12</sup>. It has been observed that<sup>11,13</sup> women who dressed themselves in black covering their hands and face had lower 25-OHD levels. Vitamin D deficiency has also been reported in pregnant woman among Muslim populations from tropical countries in whom the practice of purdah might have played an important role<sup>14,15</sup>. Although more vitamin consumption is expected in frequent pregnancies, the correlation between the number of pregnancies and vitamin D deficiency has not been reported. In a study from Pakistan<sup>15</sup>, high prevalence of vitamin D deficiency in breast-fed infants and nursing mothers were observed in 55 per cent of infants and 45 per cent of nursing

mothers. Preterm infants [20-30% of very low birth weight (<1500 g) and 60-75 per cent of extremely low birth weight babies (<1000 g)] are at risk of developing osteopaenia of prematurity due to poor intestinal absorption of calcium and impaired conversion of vitamin D into its active metabolites and their serum vitamin D levels are usually low or borderline<sup>16</sup>. Finally, the lack of adequate training of physicians in a rickets-free era coupled with the lack of adequate recommendations for vitamin D supplementation by professional organizations may also contribute to the development of rickets in exclusively breast-fed babies<sup>17</sup>.

### Breast-feeding and vitamin D deficiency

It has been estimated that breast milk from a vitamin D replete mother contains between 20 and 60 IU/l of vitamin D<sup>18</sup> and hence adequate intake of vitamin D cannot be met with human milk as the sole source of vitamin D in a breast-feeding infant<sup>18,19</sup>. In a study by Rothberg *et al*<sup>20</sup>, lactating mothers were administered daily supplements of 500 and 1000 IU of vitamin D from delivery and in spite of this, 25-OHD levels of their infants measured at six weeks were not altered. In contrast, daily supplements of 400 IU of vitamin D to infants significantly increased the 25-OHD levels at six weeks. A study from Finland<sup>21</sup> had concluded that when the mothers were supplemented with 2000 IU of vitamin D, their infants had 25-OHD levels similar to those receiving daily supplements of 400 IU of vitamin D indicating that it is more efficient to supplement infants rather than their mothers.

A study from China<sup>12</sup>, had observed that daily supplementation of breast-fed infants with either 100, 200 or 400 IU of vitamin D was not sufficient to maintain optimal levels of 25-OHD in infants especially those living in parts of the country where sunlight exposure was insufficient. Also it has been shown that the mean serum 25-OHD concentration of breast-fed infants in winter was significantly lower than that in bottle-fed infants in summer<sup>22</sup>. In most societies, vitamin D sufficiency is maintained through the conversion of 7-dehydrocholesterol to vitamin D in the skin under the influence of UV radiation from sunlight. The risk of vitamin D deficiency is heightened by the recommendations from the American Academy of Pediatrics (AAP)<sup>23</sup> that infants less than 6 months of age should be kept out of direct sunlight, children's activities should minimize sunlight exposure and protective clothing and sunscreens should be used. It is clear that many health professionals do not consider

the need for vitamin D supplementation even in at-risk groups. A study of paediatricians in the United States found that less than 50 per cent recommended vitamin D supplementation of all breast-fed infants<sup>24</sup>. Aggravating the situation is the possible resistance to vitamin D supplementation from the mothers themselves and from breast-feeding support groups, as it is perceived that vitamin D supplementation detracts from the message that breast milk is a complete food that requires no further supplementation.

### Sunlight and vitamin D

One of the potential sources of vitamin D synthesis is in the skin from the UV-B fraction of sunlight. Our traditional practice of oil massage and sunbath to the baby helps in the synthesis of vitamin D in the skin. Two hours is the required minimum weekly period of exposure to sunlight for infants if only the face is exposed, or 30 min if the upper and lower extremities are exposed<sup>25</sup>. Reduced exposure to sunlight occurs during the months of winter and due to lifestyle or cultural practices that decrease the time spent outdoors and when clothing covers more of the body surface. The effects of sunlight exposure also decreases for individuals with darker skin pigmentation and by the use of sunscreens and all of these factors make it very difficult to determine what is the adequate sunlight exposure for any given infant or child<sup>26</sup>. However intense exposure to solar ultra violet rays during childhood and adolescence increases a person's risk of developing melanoma and basal cell carcinoma. Therefore American Academy of Pediatrics<sup>27,28</sup> recommends paediatricians to incorporate skin protection counselling into practice in order to achieve the following objectives: (i) increase the proportion of people who use at least one of the following protective measures that might reduce the of skin cancer *i.e.*, avoiding the sun between 10:00 and 16:00 h, wearing sun-protective clothing when exposed to the sun, using sunscreen with a sun protection factor (SPF) of >15, and avoiding artificial sources of UV light, and (ii) reducing the deaths from melanoma to 2.5 per 100 000 people<sup>29</sup>.

### Clinical manifestations of vitamin D deficiency

The newborn infant born to a vitamin D replete mother is protected from vitamin D deficiency for the first few months of life as 25-OHD crosses the placenta readily and neonatal levels approximate two thirds of maternal serum concentrations. Serum 25-OH D has a half-life of approximately 3 wk, thus providing some

protection against vitamin D deficiency for a couple of months even if the young infant does not receive vitamin D whereas in an infant who is exclusively breast-fed and who gets minimal sunlight exposure or an infant who is on a non fortified milk substitute runs the risk of developing vitamin D deficiency rickets by 4-6 months of age. Hence supplementation should begin within the first 2 months of life<sup>23</sup>. Vitamin D deficiency in infancy may be symptomatic or asymptomatic. The clinical presentation of nutritional rickets is stage dependent and depends on the duration of the vitamin D deficiency. Hypocalcaemic symptoms determine the clinical spectrum in stage I, skeletal deformities become obvious in stage II and worsen in stage III, when hypocalcaemic symptoms also occur<sup>30</sup>. Symptomatic vitamin D deficiency manifests as craniotabes, rickety rosary, swelling of the ends of long bones, frontal bossing of the skull, hypocalcaemic seizures or tetany and slow motor development.

In a series of cases of hypocalcaemia in early infancy reported from Turkey, majority was due to vitamin D deficiency in exclusively breast-fed infants<sup>30</sup>. Symptomatic hypocalcaemia in young infants due to vitamin D deficiency has been reported in two studies from UK<sup>31,32</sup>. A case series of 13 exclusively breast-fed infants presenting with hypocalcaemic seizures with proven vitamin D deficiency has been reported from India<sup>33</sup>. Of these 13 infants, the youngest was 2 months old and the oldest being 6 months. The nutritional status of all these infants was normal and all were born at term and none of them had received vitamin D supplements. Clinical signs of rickets (rachitic rosary and craniotabes) were observed in one of these 13 infants whereas radiological features in only two of them. Since the vast majority of our patients presented with hypocalcaemic seizures with minimal skeletal deformities, they had stage I nutritional rickets. Vitamin D deficiency in all the mothers of these infants was biochemically proven with low 25- OHD levels and none of these mothers exhibited any overt clinical abnormality. Dilated cardiomyopathy and myelofibrosis<sup>34</sup> were the complications reported in the study. Dilated cardiomyopathy as a complication of vitamin D deficiency rickets responding to vitamin D therapy has been reported in earlier studies<sup>35,36</sup>. The classical radiological features of rickets include generalized osteopaenia, widening of the growth plates, and cupping of metaphyseal regions of long bones<sup>37</sup> though other studies had reported that vitamin D deficiency can occur in infants and children without radiological evidence because of the increased metabolic

demands due to rapid growth resulting in hypocalcaemia before any radiological changes could occur<sup>31</sup>.

Although hypocalcaemia in early infancy is commonly associated with functional or organic hypoparathyroidism, vitamin D deficiency and/or nutritional rickets should be considered in the differential diagnosis and measurement of serum 25-OHD levels should be included in the workup of hypocalcaemia<sup>30</sup>. Rickets during infancy has been associated with higher prevalence of lower respiratory tract infections<sup>38</sup>, which remain one of the largest causes of infant mortality in India. The long-term consequences of vitamin D deficiency rickets are increased risk for type 1 diabetes mellitus, cancer and osteoporosis<sup>24</sup>.

### Diagnosis

The diagnosis of rickets is based on its characteristic clinical and biochemical findings. Vitamin D deficiency results in hypocalcaemia, hypophosphataemia, elevated alkaline phosphatase levels and secondary hyperparathyroidism. Tsang<sup>39</sup> had reported that a low phosphate level combined with a low 25-hydroxyvitamin D concentration and radiologic evidence of rickets confirms the diagnosis of vitamin D deficiency rickets. Based on serum 25-OHD concentrations<sup>40</sup>, vitamin D deficiency is classified as:

*Mild vitamin D deficiency:* Serum 25-OHD concentration of 25-50 nmol/l. Serum levels over 50 nmol/l prevent secondary hyperparathyroidism and elevated alkaline phosphatase levels.

*Moderate vitamin D deficiency:* Serum 25-OHD concentration of 12.5-25 nmol/l. The incidence of hypocalcaemia and rickets increases with moderate deficiency.

*Severe vitamin D deficiency:* Serum 25-OHD concentration less than 12.5 nmol/l. Vitamin D concentrations less than 12.5 nmol/l are seen in over 70 per cent of children with rickets and over 90 per cent of children with hypocalcaemia.

However, the cut-off for hypovitaminosis D in neonates is still being debated. Zeghoud *et al*<sup>41</sup> found neonatal 25-OHD concentrations <30 nmol/l (12 ng/ml) be associated with elevated parathyroid hormone (PTH) and hence proposed that concentration as the cut-off for diagnosing hypovitaminosis D in the newborn. Concentrations of calcitriol may be low, normal or high at the time of diagnosis and hence is of no value in making the diagnosis.

### Treatment

High dose vitamin D therapy (stoss therapy) is an effective method for treating established or recalcitrant vitamin D deficiency. It involves oral or intramuscular administration of the total treatment dose of vitamin D 600 000 IU either as a single dose (as this produces rapid healing allowing earlier differential diagnosis from genetic vitamin D resistant rickets) or as oral vitamin D3 at a dose of 2000-6000 IU producing radiologic clearing in 2-4 wk<sup>42</sup>. Akcam *et al*<sup>43</sup> had observed that the increase in bone mineral densities with two different therapy regimens of vitamin D [either a single dose of vitamin D (600,000 IU) or 20,000 IU/day given orally for 30 days] in infants with vitamin D deficiency rickets was similar and not superior to each other.

### Prevention

Vitamin D deficiency continues to be a public health problem in many countries despite the availability of cheap and effective means to prevent this disease. Sources differ as to the appropriate time frame to begin supplementation, beginning as early as birth to 2 months of age and also with the dose. Vitamin D supplementation to all infants should begin during the first days of life as there is a high risk of sub clinical vitamin D deficiency, even in regions with a temperate climate<sup>22</sup>. Vitamin D deficiency in exclusively breast-fed infants up to 6 months of age can be prevented by the following measures: supplementing vitamin D to all pregnant and lactating mothers, supplementing vitamin D to all exclusively breast-fed infants and exposing all pregnant and lactating women and their infants to sunlight. At present, vitamin D supplementation is not a part of antenatal care/Integrated Management of Neonatal & Childhood Illness (IMNCI) programmes in India. In a study by Pittard *et al*<sup>44</sup> in preterm and term infants whose mothers had normal 25-OHD levels, supplementation with daily doses of 400 and 800 IU of vitamin D were compared and it was concluded that daily dose of 400 IU was sufficient to achieve normal serum 25-OH D levels. Recently the American Academy of Pediatrics (AAP) has recommended a supplement of 200 IU of vitamin D for the following<sup>23</sup>: (i) All breast-fed infants unless they are weaned to at least 500 ml/day of vitamin D fortified formula; (ii) All non breast-fed infants who are ingesting less than 500 ml/day of vitamin D fortified milk/formula; and (iii) Children and adolescents who do not get regular sunlight exposure, do not ingest at least 500 ml/day of vitamin D fortified milk or do not take a daily multivitamin supplement containing at least 200 IU of vitamin D.

Although vitamin D supplementation appears as a safe, low cost and reasonable option, Greer and Marshall<sup>45</sup> reported that there was no evidence of vitamin D deficiency occurring in vitamin D non supplemented breast-fed infants during the first 6 months of life. However, large trials studying the effects of vitamin D supplementation on substantive neonatal and maternal outcomes and comparing different dosage schedules should be conducted in order to clarify further the role of vitamin D supplementation. In addition, primary care providers need to provide ongoing patient and public education regarding the need for supplementation, stressing that the concept of “breast is best” should not override routine supplementation with vitamin D and increasing exposure to sunlight.

### Conclusion

With the renewed worldwide emphasis on exclusive breast-feeding of infants for the first 6 months of life, infants even in developing countries are at risk of developing vitamin D deficiency unless adequate preventive measures are taken. Predisposing factors include reduced exposure to sunlight in spite of this being available in plenty in a country like India, due to various social and cultural reasons. There is a need to consider implementation of a vitamin D Supplementation Programme in infancy at the community level. Nutritional rickets in early infancy may become a more widespread problem in the near future unless strategies to ensure optimal vitamin D status for pregnant women and newborns are developed.

### References

- Lauer JA, Betran AP, Barros AJ, de onis M. Deaths and years of life lost due to suboptimal breast feeding among children in the developing world: a global ecological risk assessment. *Public Health Nutr* 2006; 9 : 673-85.
- Institute of Medicine, Food and Nutrition Board, Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. Vitamin D. In: *Dietary reference intakes for calcium, phosphorus, magnesium, vitamin D, and fluoride*. Washington, DC: National Academy Press; 1997. p. 250-87.
- Mahomed K, Gulmezoglu AM. Vitamin D supplementation in pregnancy. *Cochrane Database Syst Rev* 2000 (2): CD000228. DOI:10.1002/14651858.CD000228.
- Henderson A. Vitamin D and the breast-fed infant. *J Obstet Gynecol Neonatal Nurs* 2005; 34 : 367-72.
- Dawodu A, Agarwal M, Hossain M, Kochiyil J, Zayed R. Hypovitaminosis D and vitamin D deficiency in exclusively breast-feeding infants and their mothers in summer: a justification for vitamin D supplementation of breast-feeding infants. *J Pediatr* 2003; 142 : 169-73.
- Atiq M, Suria A, Nizami SQ. Vitamin D status of breastfed Pakistani infants. *Acta Paediatr* 1998; 87 : 737-40.
- Ho ML, Yen HC, Tsang RC, Specker BL, Chen XC, Nichols BL. Randomized study of sunshine exposure and serum 25-OHD in breast fed infants in Beijing, China. *J Pediatr* 1985; 107 : 928-31.
- Salle BL, Delvin EE, Lapillonne A, Bishop NJ, Glorieux FH. Perinatal metabolism of vitamin D. *Am J Clin Nutr* 2000; 71 (Suppl) : 1317S-24S.
- Krishnamachari KA, Iyengar L. Effect of maternal malnutrition on the bone density of neonates. *Am J Clin Nutr* 1975; 28 : 482-6.
- Anast CS, Carpenter TO, Key LL. Metabolic bone disorders in children. In: Avioli LV, Krane SM, editors. *Metabolic bone disease and clinically related disorders*. Philadelphia: Saunders; 1990. p. 850-84.
- Pehlivan I, Hatun S, Aydogan M, Babaoglu K, Gokalp AS. Maternal vitamin D deficiency and vitamin D supplementation in healthy infants. *Turk J Pediatr* 2003; 45 : 315-20.
- Specker BL, Ho ML, Oestreich A. Prospective study of vitamin D supplementation and rickets in China. *J Pediatr* 1992; 120 : 733-9.
- Alagöl F, Shihadeh Y, Boztepe H, Azizlerli H, Sandalcı O. Sunlight exposure and vitamin D deficiency in Turkish women. *J Endocrinol Invest* 2000; 23 : 173-7.
- Rab SM, Baseer A. Occult osteomalacia amongst healthy and pregnant women in Pakistan. *Lancet* 1976; 2 : 1211-3.
- Atiq M, Suria A. Maternal vitamin-D deficiency in Pakistan. *Acta Obstet Gynecol Scand* 1998; 77 : 970-3.
- Singh M. Metabolic disorders . In. Singh M, editor. *Care of the newborn*. New Delhi: Sagar Publications; 2004, p. 353-75.
- Cara FJ. Vitamin D deficiency rickets in breast fed infants. Available from: [http://www.medscape.com/view\\_article/420205](http://www.medscape.com/view_article/420205), accessed on May 15, 2007.
- Hollis BW, Roos BA, Draper HH. Vitamin D and its metabolites in human and bovine milk. *J Nutr* 1981; 111 : 1240-8.
- Reeve LE, Chesney RW, DeLuca HF. Vitamin D of human milk :identification of biologically active forms. *Am J Clin Nutr* 1982; 36 : 122-6.
- Rothberg AD, Pettifor JM, Desmond FC. Maternal infant vitamin D relationships during breast-feeding. *J Pediatr* 1982; 101 : 500-3.
- Ala-Houhala M. 25-Hydroxyvitamin D levels during breast-feeding with or without maternal or infantile supplementation of vitamin D. *J Pediatr Gastroenterol Nutr* 1985; 4 : 220-6.
- Cabezuelo Huerta G, Vidal Micó S, Abeledo Gómez A, Frontera Izquierdo P. 25-Hydroxyvitamin D levels in infants. Relation with breast-feeding. *Ann Pediatr* 2007; 66 : 491-5.
- Gartner ML, Greer RF. Prevention of rickets and Vitamin D deficiency: New guidelines for vitamin D intake section on breastfeeding and committee on nutrition. *Pediatrics* 2003; 111 : 908-10.
- Davenport ML, Uckun A, Calikoglu AS. Pediatrician patterns of prescribing vitamin supplementation for infants: Do they contribute to rickets. *Pediatrics* 2004; 113 : 179-80.
- Specker BL, Valanis B, Hertzberg V, Edwards N, Tsang RC. Sunshine exposure and serum 25-hydroxyvitamin D

- concentrations in exclusively breast-fed infants. *J Pediatr* 1985; 107 : 372-6.
26. Fuller KE, Casparian JM. Vitamin D: balancing cutaneous and systemic considerations. *South Med J* 2001; 94 : 58-64.
  27. American Academy of Pediatrics. Committee on Environmental Health. Ultraviolet light: a hazard to children. *Pediatrics* 1999; 104 : 328-33.
  28. Etzel RA, Balk SJ, editors. *Pediatric environmental health*. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2003.
  29. US Department of Health and Human Services. Objectives for Improving Health (Part A: Focus Areas 1-14), Cancer. In: *Healthy people 2010* (conference ed, Vol 1). Washington, DC: US Department of Health and Human Services; 2000. Available at: [www.health.gov/healthypeople/Document/pdf/Volume1/03Cancer.pdf](http://www.health.gov/healthypeople/Document/pdf/Volume1/03Cancer.pdf), accessed on May 4, 2007.
  30. Hatun S, Ozkan B, Orbak Z, Doneray H, Cizmecioglu F, Toprak D, et al. Vitamin D deficiency in early infancy. *J Nutr* 2005; 135 : 279-82.
  31. Ladhani S, Srinivasan L, Buchanan C, Allgrove J. Presentation of vitamin D deficiency. *Arch Dis Child* 2004; 89 : 781-4.
  32. Pal BR. Rickets resurgence in the United Kingdom: improving antenatal management in Asians. *J Pediatr* 2001; 139 : 337-8.
  33. Balasubramanian S, Shivbalan So, Saravanakumar P. Hypocalcemia due to vitamin D deficiency in exclusively breast fed infants. *Indian Pediatr* 2006; 43 : 247-51.
  34. Balasubramanian S, Varadharajan R, Ganesh R, Shivbalan So. Myelofibrosis and vitamin D deficient rickets - a rare association. *Indian Pediatr* 2005; 42 : 482-4.
  35. Olgun H, Ceviz N, Ozkan B. A case of dilated cardiomyopathy due to nutritional vitamin D deficiency rickets. *Turk J Pediatr* 2003; 45 : 152-4.
  36. Abdullah M, Bigras JL, McCrindle BW. Dilated cardiomyopathy as a first sign of nutritional vitamin D deficiency rickets in infants. *Can J Cardiol* 1999; 15 : 699-701.
  37. Mughal MZ, Salama H, Greenaway T, Laing I, Mawer EB. Florid rickets associated with prolonged breast feeding without vitamin D supplementation. *BMJ* 1999; 318 : 39-40.
  38. Muhe L, Lulseged S, Mason KE, Simoes EA. Case-control study of the role of nutritional rickets in the risk of developing pneumonia in Ethiopian children. *Lancet* 1997; 349 : 1801-4.
  39. Tsang R. Endocrinology update for pediatricians. Vitamin D-deficiency rickets. *Presented at the Annual Meeting of the American Academy of Pediatrics*; October 29, 2000; Chicago, Illinois.
  40. Munns C, Zacharin RM, Rodda PC, Batch JA, Morley R, Cranswick NE, et al. Prevention and treatment of infant and childhood vitamin D deficiency in Australia and New Zealand: a consensus statement. *Med J Aust* 2006; 185 : 268-72.
  41. Zeghoud F, Vervel C, Guillozo H, Walrant-Debray O, Boutignon H, Garabedian M. Subclinical vitamin D deficiency in neonates: definition and response to vitamin D supplements. *Am J Clin Nutr* 1997; 65 : 771-8.
  42. Heird CW. Vitamin deficiencies and excesses. In: Behrman ER, Kliegman MR, Jenson BH, editors. *Nelson text book of pediatrics*. Philadelphia: Saunders; 2004. p. 177-90.
  43. Akcam M, Yildiz M, Yilmaz A, Artan R. Bone mineral density in response to two different regimes in rickets. *Indian Pediatr* 2006; 43 : 423-7.
  44. Pittard WB, Geddes KM, Hulsey TC. How much vitamin D for neonates? *Am J Dis Child* 1991; 145 : 1147-9.
  45. Greer FR, Marshall S. Bone mineral content, serum vitamin D metabolite concentrations, and ultraviolet B light exposure in infants fed human milk with and without vitamin D2 supplements. *J Pediatr* 1989; 114 : 204-12.

*Reprint requests:* Dr S. Balasubramanian, Senior Consultant Pediatrician, Kanchi Kamakoti CHILDS Trust Hospital  
12-A, Nageswara Road, Nungambakkam, Chennai 660 034, India  
e-mail: sbsped53@sify.com