Vitamin D-Deficiency Rickets in Saudi Arabia

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Rickets was primarily a disease of temperate countries but after a long period of eradication it has reappeared among the immigrants in these countries (1–5). In sunny countries, rickets is being seen in such a magnitude as to be considered a community health problem (6–14). The natural and main source of vitamin D even in temperate countries is still through exposure to sunshine (15–17). This chapter reviews the factors associated with development of rickets in a country, Saudi Arabia, where there is abundance of sunshine.

EFFECTS OF VITAMIN D DEFICIENCY

The initial outcome of vitamin D deficiency is hypocalcemia, followed by hypophosphatemia, and a rise of alkaline phosphatase, these findings are termed biochemical rickets or osteomalacia. The hypophosphatemia, although an invariable finding in vitamin D-deficiency rickets, might not be as striking as is the hypocalcemia in the early stage of the disease (18). The hypocalcemia stimulates the parathormone which in turn leads to bone resorption in an attempt to maintain normal serum calcium (19). In growing bones, bone matrix continues to be produced but due to impaired calcification its accumulation becomes irregular leading to widening at the epiphyseal ends of the bones which manifests clinically in areas of fast bone growth like the wrist and costochondral junction. In weight-bearing long bones, inadequate mineralization may induce deformities of varying severity.

PATHOGENESIS OF RICKETS

In Riyadh, the level of ultraviolet rays available in the atmosphere is consistent with what is expected at such an altitude (20) and the amount that reaches the usually exposed human skin is enough to maintain adequate circulating levels of 25(OH)D (21). Then why do we see rickets in such a place? In trying to answer this question I will first discuss the interrelations of vitamin D status between mother and infant and then the factors affecting it.
Maternal Vitamin D Deficiency as a Cause of Rickets in Infants

In Riyadh, rickets commonly occurs in the first year of life with a mean age of ten months (6,22). Although congenital rickets has been reported (23,24) the youngest infant seen with clinical rickets in our series was two months old and presented with hypocalcemic convulsions associated with minimal bony changes (22). The mothers of rachitic infants were found to be vitamin D deficient (25) and paired maternal and cord blood vitamin D status proved to be low (26,27). In spite of this low 25(OH)D, calcium levels in cord blood were maintained within normal levels, and were even higher than the corresponding maternal levels (28,29). These findings conform with the active transplacental transport of calcium (30,31), which could be linked to the high levels of 1,25(OH)2D during pregnancy (32,33) especially since the placenta (34) and the fetus (35) can act as additional sites for the synthesis of 1,25(OH)2D. Indeed our data show normal to high levels of 1,25(OH)2D in pregnancy in spite of the low levels of 25(OH)D. A lack of correlation between the two metabolites was also shown (36).

The active transplacental calcium transfer in spite of the poor vitamin D status of the mother was found to maintain adequate fetal bone mineralization and prevent congenital rickets except in states of severe maternal osteomalacia (37).

The maternal vitamin D deficiency state during pregnancy leads to delivery of infants with poor vitamin D stores, but marginally adequate calcification. After birth these infants are unable to maintain normal calcium levels due to the loss of the active transplacental calcium pump and lack of vitamin D reserves. This might manifest as neonatal hypocalcemia in some (30,38) or later manifestations in others, depending on vitamin D content of the milk and environmental exposure to the sun (39). The evidence available supports the hypothesis that maternal vitamin D deficiency contributes to rickets in the offspring (6) (Fig. 1). Infantile rickets in Libya was attributed to similar low maternal and cord blood 25(OH)D levels (40).

Environmental Factors Leading to Vitamin D Deficiency

Housing

Most of the rachitic infants were living either in flats or traditional mud houses (6,24). The traditional mud house is high walled with small high windows. In both types of dwellings there is no direct access to sunshine in contrast to rural houses that have courtyards where mothers and their children can be exposed to sunlight in privacy (6). The lowest levels of vitamin D among the pregnant mothers were found to be associated with traditional houses and flats (29).

Location

The location of the house may also contribute to vitamin D deficiency. This is supported by the finding that almost all the rachitic infants came from the crowded
parts of the city (27). In these areas, mothers and their infants remain indoors with no chance of being exposed to sunshine. This simulates what used to be seen in Europe following the industrial revolution when rickets was endemic in the slums of the industrial cities (2), although in Riyadh there is no lack of ultraviolet rays (21,22) but only lack of exposure to it.

**Customs**

**Female dressing**

Since the purdah observed by some immigrants in Europe was considered to be a major factor in the prevalence of rickets and osteomalacia among them we studied the pattern of dressing and its relation to the occurrence of rickets. The traditional dressing of women in Riyadh was found not to affect their vitamin D status as the 25(OH)D levels of female students were found to be similar to male students (41). Also, school girls from the age of six to nineteen years did not show a drop in 25(OH)D levels coinciding with the change to traditional dress taking place at puberty (42). In rural areas, where women wear similar traditional dress, rickets is not a problem (6,43). This could easily be explained by the fact that houses have courtyards where sun exposure can be achieved while carrying out home duties. From the available evidence it can thus be stated that the women’s way of dressing *per se* is not what causes vitamin D deficiency.
Wrapping the infants

Although we have reported this custom as a causal factor of rickets in our original communication (6), subsequently we did not find evidence to support this, especially since the period of wrapping is up to four months of age. In this period of life mothers do not usually expose their infants to direct sunshine guided by the belief that the sun will hurt them (39).

The Umbrella Phenomenon

The sunshine is abundant in Riyadh but an umbrella is formed depriving the infants and their mothers from getting access to sunshine (44). Urbanization forms the main pillar on which this umbrella is pivoted as shown in Figure 2. Urbanization is associated with living in flats that are devoid of sunshine especially since ultraviolet light does not penetrate glass. Rickets is seen due to man-made factors preventing access to the available ultraviolet rays and accordingly synthesis of vitamin D. The statement by Park (45) before the discovery of vitamin D that rickets is a disease of artificial ways of living and never associated with natural life still holds true in sunny countries.

EPIDEMIOLOGY

As rickets is seen in Riyadh at a mean age of ten months and the usual presentation is by symptoms not directly related to the disease (Fig. 3), its diagnosis might be missed and, accordingly, the true incidence is difficult to elicit (6). The diagnosed
cases formed less than 1% of the admission in Riyadh children's hospitals (unpublished data). The majority of the rachitic infants have normal protein and caloric nutritional status (24). This makes it sometimes difficult to elicit the physical signs of rickets like swollen wrists and costochondral beading. In an epidemiological and clinical study of the patients seen by the author, 52% were living in flats with a majority of illiterate mothers. Fifty-seven percent of the mothers thought that exposure to the sun was harmful to their infants and only 12% realized that sunlight was good for the infant. Eighty-six percent of the mothers never exposed their infants to the sun. Parents were first degree cousins in 46% which is not different from the general community. Eighty-nine percent of rachitic children were breast-fed. These facts confirm our previous observations (6).

CLINICAL PICTURE

The clinical presentation of rickets in cases seen by the author in a period of three years is shown in Figure 3. These infants present with respiratory and gastrointestinal symptoms and signs of rickets may pass unnoticed. Craniotabes is elicited only in early life. During the first six months of life, rickets may present with hypotonia and hypocalcemic convulsions. At this stage, rickets is subclinical, and radiology of the bones of the forearm may reveal either minor changes or no changes at all. The hypocalcemic convulsions may be precipitated by fever. In the second year of life delayed walking and eruption of teeth may warrant seeking medical advice. It is only when the child starts to walk that bowing of the legs and a waddling gait becomes an obvious cause of concern. Excessive sweating may be noticed by some parents.
DIAGNOSIS

Diagnosis of rickets in infants depends mainly on suspecting the condition and accordingly looking for its signs among children presenting with the common pediatric ailments such as chest infection and gastroenteritis.

PREVENTION

In such sunny countries, exposure to the sun is the natural and best method of preventing rickets. This can be achieved by alleviating the factors forming the umbrella. Houses need to be designed in a way to allow for exposure to sun in privacy. When exposure to the sun is impractical vitamin D supplementation in the form of medication is essential, 400 IU daily is enough to prevent rickets. Improvement of maternal vitamin D status will prevent neonatal hypocalcemia (39) and will render breast-fed infants not needing further supplementation and maintain bone mineralization for at least the first six months of life without vitamin D supplementation (46). For complete discussion of this important topic see chapter by L. Paunier.

REFERENCES


DISCUSSION

Dr. Holick: You made a very good point regarding the role of breast-feeding in vitamin D nutrition. It may be worthwhile to mention that the mechanism by which transfer from mother to child is not specifically by secreting vitamin D into the milk, but rather by passive transport in the milk of both albumin and the vitamin-D-binding protein that carries with it principally 25(OH)D, which is then the principal source of vitamin D for the infant.

Dr. Coates: Malnourished babies usually don't have a regular medical follow-up, and they come to the hospital with an infection such as pneumonia or acute diarrhea which gets prolonged because of secondary lactase deficiency. Nutritional rickets is diagnosed at the hospital. We often see hypocalcemia with convulsion after fasting, in first and third stage rickets. What is your experience regarding rickets with malnutrition after prolonged diarrhea?

Dr. Elidrissy: Most cases of rickets occur among breast-fed, well nourished infants. I have also seen cases of malabsorption and celiac disease who developed rickets. But as a whole, in our community, the nutrition status of infants is good. And they might develop rickets as part of chronic diarrhea, yes, but this is not the general case. The incidence of rickets is about 2 to 3% in a hospital population so that we see about 500 children with rickets per year. The other problem is hypocalcemia in the first months of life. I have seen one or two cases of hypocalcemic convulsions with florid rickets, but most of the cases occur at an early stage and with high fever. Thus, as a rule, every patient admitted for febrile convulsions ought to have a work-up to eliminate a disturbance in calcium homeostasis.

Dr. Pettifor: I have two comments. The first is over the term vitamin D deficiency. It should be reserved for those individuals that have other biochemical evidence of inadequate vitamin D supply, in other words, not only low 25(OH)D but also hypocalcemia, elevated PTH levels, and perhaps hypophosphatemia; and that we should reserve for those who have just low 25(OH)D levels the term low vitamin D status rather than vitamin D deficiency. I think this may help us to differentiate the problem in various countries, for instance Saudi Arabia. Do your mothers actually have clinical symptoms or biochemical evidence of vitamin D deficiency or do they not rather just suffer from low vitamin D status? I think this makes a difference. Secondly, I believe that there is no harm in suggesting that we should give vitamin D supplements not only to all breast-fed infants, but to all infants under the age of one year. As pediatricians, the majority of us are attempting to encourage breast-feeding. Yet, to suggest that only breast-fed infants need vitamin D supplementation is probably going to have a negative effect on our efforts. Even if infants receive vitamin D enriched formulas, there is no evidence that an extra 400 IU vitamin D/day as a supplement is going to produce vitamin D toxicity. Thus to recommend vitamin D supplementation to all infants would simplify the message and the public health strategies. To ensure that mothers and their infants receive adequate sunlight to prevent vitamin D deficiency without vitamin D supplementation may be a major problem in certain areas where social customs strongly prevent going out of doors during pregnancy.

Dr. Elidrissy: We have just finished a nationwide study on the levels of vitamin D in Saudi Arabia. Levels of 25(OH)D are very low compared to the levels reported in the United States or Europe. Thus, as already discussed, in sunny countries levels of vitamin D may be on the low side depending on environmental factors. We now recommend in Saudi Arabia that all breast-fed infants be given vitamin D supplementation, and the same is recommended by the Ministry of Health for all pregnant women.

Dr. Glorieux: In keeping with the title of this particular session, which is "Rickets as a
Public Health Problem,” could you give us some indication, whether in Saudi Arabia rickets is a significant factor of morbidity, in terms of admission to hospitals, growth retardation, residual deformities, and other problems that may arise from having been rachitic at an early age.

Dr. Elidrissy: There appear to be no long-term effects of rickets, in our community. My colleagues and I have also asked certain obstetricians about the incidence of the so-called rachitic pelvis, but no case was noted. Serious problems may be encountered in infants with rickets who are admitted for convulsions and pulmonary infection. Adequate preventive measures is the best way to avoid them.

Dr. Heinrich: In terms of public health, where do you put the detection limit of rickets? Is it a clinical or a biochemical one? When do you have to implement the preventive measures? You also said that there is no malnourishment. What about calcium intake in these children? Could they be calcium deprived?

Dr. Elidrissy: All the cases which we have seen were showing evidence of clinical rickets. With regard to the low calcium intake, all these infants are breast-fed, and I assume that they receive enough calcium. But of course, in order to absorb that calcium, it is imperative that they receive enough vitamin D.

Dr. Markestad: It is interesting that the same clinical pattern of rickets is seen in Saudi Arabia, Libya, and Norway, although in Norway it is not a major public health problem except in the immigrant population. In all three countries the disease is almost exclusively limited to the first 18 months of life, and permanent skeletal deformities appear to be extremely rare.

Dr. Martinez: At what age does the introduction of beikost take place in your country? The early dietary use of flours with a high content in phytate causes poor absorption of calcium as it has been seen in Bedouins, who eat a bread called raghif (1,2).

Dr. Elidrissy: It is a teaching of Koran that breast-feeding should be continued for two years. So, many mothers are resisting introduction of any other element before one year of age. I personally don’t like introducing solids, and that includes phytate or fiber containing foodstuff, before the age of six months. They, thus, should not be considered as playing a significant role in the pathogenesis of rickets.

Dr. Paunier: You said that you recommend that breast-fed infants should receive vitamin D supplements. I fully agree with that. But what is the percentage of the breast-feeding mothers who actually comply with this recommendation? And, in your country, do you have a specific education program for rickets prophylaxis?

Dr. Elidrissy: Earlier on, we recommended that people take advantage of a nice weekend in the sun. This became increasingly more difficult with urbanization. We now give 400 IU/ d of vitamin D to all breast-fed infants. The advice is included in Health Education programs but I have no data about compliance in our population.

REFERENCES