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Review

Congenital rickets due to vitamin D deficiency in the mothers

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SUMMARY

Background & aims: We wished to review all published reports of congenital rickets to identify the causes and characteristics.
Methods: 25 cases were identified in 19 published reports in which there was radiological and/or histological evidence of rickets in the first two weeks after birth. Cases of rickets associated with maternal renal failure were excluded as were infants born at less than 32 weeks gestation.
Results: There was evidence of maternal deficiency in 24 of these cases. In 16 cases the diagnosis of the rickets led to the identification of symptomatic osteomalacia in the mothers. Of the 12 mothers who had assays for serum 25-hydroxyvitamin D (25OHD) 11 had values less than 10 ng/mL. Presentations in the infants included craniotabes, wide skull sutures, rachitic rosaries, enlargement of the wrists, tetany and convulsions. In two cases rickets had been suspected from antenatal X-rays. In five cases fractures were found at the time of initial presentation. Of the 16 infants with serum calcium assays 15 had values lower than 8.8 mg/dL. Of 13 infants who had serum alkaline phosphatase assays 12 had abnormally high levels. Of the seven infants in whom serum 25OHD was measured before treatment, all had values less than 10 ng/mL.
Conclusions: These reports provide strong support for the view that maternal deficiency leads to overt bone disease from before birth. Maternal deficiency probably also leads to impairment of bone quality in postnatal life. The importance of ensuring adequate vitamin D nutrition in pregnancy is emphasised.

1. Introduction

In recent years there has been a great increase in the recognition that vitamin D deficiency is common. At one time it was thought to be a problem mainly of immigrant populations in particular western countries. Now numerous reports point to its prevalence in developed countries [1–3]. While there remains argument about the level at which deficiency is clinically important [4], it is clear that by any standard deficiency is widespread. While the best known consequences of vitamin D deficiency in childhood are rickets and hypocalcaemia there is growing evidence that deficiency also has implications for tissues other than bone [5].

Vitamin D is obtained in part from the diet but there are few foodstuffs that contain significant amounts. For most people the major source of vitamin D is its synthesis in the skin under the influence of ultraviolet B radiation. This is limited by an indoor lifestyle, higher latitudes, atmospheric pollution, the use of sunscreens, skin pigmentation and conservative dress codes [6,7].

In recent years numerous surveys in different countries of mother–neonate pairs have demonstrated that there is a close correlation between the vitamin D status of newborn infants and that of their mothers [2,8–18]. In both large surveys and individual case reports it is clear that low levels of serum 25-hydroxyvitamin D (25OHD) are often found in neonates and reflect the vitamin D status of the mothers [18,19]. If neonatal deficiency is found it is important to investigate the mother.

Vitamin D deficiency in neonates is probably more common than objective evidence of bone disease based on histology, radiology or clinical signs (such as craniotabes or rachitic rosaries). Some patients present clinically, for example with hypocalcaemic convulsions, and have no radiological evidence of rickets [20–22]. Prior to 1930 there was considerable debate about whether congenital rickets could occur [23,24]. Recent reports [25] have once again cast doubt on the view that rickets can be present at birth. In order to explore this issue we have reviewed published cases of congenital rickets over the intervening years. We felt that it

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Table 1
Case reports of vitamin D deficiency rickets in neonates and stillbirths.

Source	Infant details	Serum calcium (mg/dL)	Serum ALP	Serum 25OHD (ng/mL)	Maternal findings
Maxwell & Turnbull 1930 [23] case 1 (China)	Died aged 5 days. Severe rickets radiologically in ribs and in numerous long bones. Histology: rickets.				Bone pain 3 years. Pelvic deformity. Malnutrition.
Maxwell & Turnbull 1930 [24] case 2 (China)	Radiology: 'mild rickets' in ribs and several long bones.				Pain in limbs 3.5 years. Tetany. Fits. Serum calcium 4.7 mg/dL
Maxwell et al., 1932 [27] (China)	Rachitic rosary noted at birth. Radiology: rachitic changes in metaphyses of several long bones. GI bleed and died aged 3 days. Histology: severe rickets.				Malnutrition, bone pain 2 years. Pelvic deformity and obstructed labour. Serum calcium 7.4 mg/dL
Rector 1935 [24] (USA)	Died aged 2 days with GI bleeding. Rachitic rosary found at autopsy. Radiology: severe rachitic changes in ribs and metaphyses. Histology: rickets.				Malnutrition.
Maxwell 1935 [28] case LC (China)	Stillbirth. Radiology: rachitic changes in ribs and metaphyses. Histology: rickets				Bone pain 5 years, tetany, loss of height, hypocalcaemia. Pelvic deformity and obstructed labour. Serum calcium 7.3 mg/dL
Maxwell 1935 [28] case CUC (China)	Died *in utero* while section in progress. Radiology: rachitic changes in ribs and metaphyses.				Bone pain 10 years spontaneous fractures, Pelvic deformity and obstructed labour. Serum calcium 7.8 mg/dL
Wolfe 1935 [29] case 1 (China)	Radiology: rachitic changes in metaphyses.	8.1			Multiple episodes of tetany. Serum calcium 5.4 mg/mL
Wolfe 1935 [29] case 2 (China)	Embryotomy. Histology: rickets				Pelvic deformity and obstructed labour for 4 days. Radiology: osteomalacia. Serum calcium 8.3 mg/dL
Wolfe 1935 [29] case 3 (China)	Stillbirth. Radiology: rachitic changes in metaphyses.	5.6			Bone pain 5 years. Tetany. Serum calcium 7.8 mg/dL
Maxwell et al., 1939 [30] case TLF (China)	Fracture of left femur at 2 days. Radiology: 'marked rickets'. Tetany and facial spasm at 10 days. Fractures right femur and right ulna 11–22 days.	4.0			Bone pain 9 years. Recurrent tetany 6 months. Serum calcium 4.0 mg/dL
Begum et al., 1968 [31] case 1 (UK)	Craniotabes noted at birth. Radiology: skull fracture and rachitic changes in metaphyses.	6.3	High		Bone pain 3 years. Serum calcium 5.6 mg/dL, ALP high later found to have coeliac disease.
Begum et al., 1968 [27] case 2 (UK, West Indian)	Craniotabes noted aged 3 days. Radiology: rachitic changes in metaphyses.	5.5	High		Serum calcium 8.5 mg/dL. Later found to have biliary obstruction.
Ford et al., 1973 [32] case 2 (UK, Asian)	Craniotabes noted at birth. Radiology: rachitic changes in metaphyses.	6.8	High		Serum calcium 6.5 mg/dL, ALP high
Russell & Hill 1974 [33] (UK, Asian)	Rickets found on antenatal radiology. After birth rachitic changes at wrists confirmed.				Serum calcium 7.2 mg/dL, ALP high, 25OHD 3.0 ng/mL.
Moncrieff 1974 [34] UK, Asian)	Craniotabes, wide sutures, large fontanelle, rachitic rosary at birth. Radiology: rachitic changes at wrists.	6.7	High	8.3	Bone pain. Serum calcium 8.2 mg/dL, ALP high, 25OHD 7.2 ng/mL
Sann et al., 1977 [35] (France)	Wide sutures. Radiology: rachitic changes in metaphyses in legs.	8.2	High		Serum 25OHD 1.0 ng/mL.
Park et al., 1987 [36] case A (Germany, Turkish)	Craniotabes noted aged 12 days. Radiology: radial fracture and rachitic changes at wrists.	6.8	High	9.4	Bone pain. Waddling gait. Serum ALP high, 25OHD 5.6 ng/mL.
Teotia et al., 1995 [37] case 1 (India)	Frontal and parietal bossing, large fontanelle, enlarged wrists and ankles noted at birth. Radiology: rickets.	8.0	High	<2	Bone pain. Muscle weakness. Paraesthesiae. Pelvic deformity. Serum calcium 8.0 mg/dL, ALP high, 25OHD <2 ng/mL.
Teotia et al., 1995 [37] case 2 (India)	Craniotabes, large fontanelle, enlarged wrists. Radiology: rickets.	8.4	High	2.5	Bone pain. Muscle weakness. Paraesthesiae. Pelvic deformity. Serum calcium 6.0 mg/dL, ALP high, 25OHD 2.5 ng/mL
Teotia et al., 1995 [37] case 3 (India)	Craniotabes, wide sutures, rachitic rosary, enlarged wrist. Radiology: rachitic changes in metaphyses.	8.4	High	<2	Bone pain. Muscle weakness. Tetany. Obstructed labour. Serum calcium 5.6 mg/dL, ALP high. 25OHD 2.5 ng/mL.
Blond et al., 1997 [38] (France, Moroccan)	Craniotabes, wide sutures, enlarged wrists noted at birth. Radiology: rachitic changes at wrists.	5.6	High	4.1	Bone pain for years. Paraesthesiae. Serum calcium 7.0 ng/dL, 25OHD 2.8 ng/mL.
Maiyegun et al., 2002 [39] (Kuwait)	Craniotabes, large fontanelle, rachitic rosary noted at birth. Radiology: fractures of ribs and femora, rachitic changes in metaphyses.	Normal	High	<5	Serum ALP high, 25OHD 5.1 ng/mL.
Innes et al., 2002 [40] case 1 (Canada, Cree)	Abnormalities found in antenatal radiology, wide sutures noted at birth. Radiology: rachitic changes at wrists. Femoral fractures later	7.7	Normal		Seizures. Serum calcium 7.6 mg/dL, ALP high, 25OHD 14.8 ng/mL
Mohapatra et al., 2003 [41] (India)	Craniotabes, rachitic rosary, enlarged wrists. Tetany aged 3 days. Radiology: rachitic changes in metaphyses.	6.6	High		Serum calcium 4.3 mg/dL, ALP high, 25OHD 2.9 ng/mL. Radiology: 'osteomalacia'
Soler-Bel et al., 2011 [42] (Spain, Moroccan)	Stillbirth. Wide sutures, rachitic rosary and rib fractures found at autopsy. Radiology: rachitic changes in long bones. Histology: rickets.				Bone tenderness. Recurrent tetany for 6 months. Serum calcium 5.5 mg/dL, 25OHD 7.1 ng/mL. Later found to have coeliac disease.

Abbreviations: 25OHD = 25-hydroxyvitamin D, ALP = Alkaline phosphatase.
Conversion factors to SI units: Serum calcium: 4 mg/dL = 1 mmol/L, Serum 25OHD: 1 ng/mL = 2.5 nmol/L.