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*CASE REPORT*

# Rickets in the Benelux. A case report of two Indian immigrants

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**The last decades showed a resurgence of rickets and osteomalacia in the developed countries.**
**In this report, we present two cases of dietary rickets in Indian teenage brothers who migrated to Europe. Supplementation of calcium and vitamin D3 to their diet resulted in rapid relief of musculoskeletal symptoms.**

**Keywords** : rickets ; immigrants.

## INTRODUCTION

Rickets in young children and osteomalacia in adults are caused by inadequate intake or uptake of calcium and/or phosphorus, which occurs in a vitamin D deficiency state. A lack of vitamin D due to insufficient exposure of the body to sunlight, inadequate dietary intake or renal disease leads to an excess of non-mineralised osteoid. Eventually mechanical insufficiency and bone deformities occur (*9*).

In developed countries, rickets and osteomalacia were thought to be eradicated since the discovery of vitamin D and the role of sunlight in vitamin D formation. However, in the second half of the 20th century a resurgence of the disease was seen in Europe and the United States. Beck-Nielsen *et al* described 112 patients with rickets of which 74% were immigrants (*1*). Reported cases of nutritional rickets in the United States increased from 65 between 1975-1985 to 166 between 1986-2003 (*7*). Immigration of dark skinned immigrants to high latitude countries, malnutrition and avoidance of sunlight to reduce the risk of skin cancer, are thought to be probable causes (*7, 8*).

In this report, two Indian brothers with painful myopathy and limb deformities are presented.

## CASE REPORT

Two Indian brothers were living in The Netherlands since two years, following a religious program in a nearby monastery. Both were strict vegetarians and disliked Dutch milk. They spent most of their time indoors, engaging in religious activities.

The first patient, a 12-year-old male, presented with a waddling gait, muscular weakness and bone pain. History revealed a fracture of the radius and ulna. His estimated calcium-intake was 100 mg/day.

Upon physical examination, hip function was limited and painful on both sides. Trendelenburg's

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sign was positive on both sides. Also Gowers' sign was positive ; he rose from his chair by climbing up his legs. Neurological examination was normal.

Initial laboratory testing revealed a low serum calcium of 1.9 mmol/L (normal range : 2.1-2.6 mmol/L), an elevated alkaline phosphatase level of 2,133 U/L (normal range : < 140 U/L) and an elevated parathyroid hormone of 715 pmol/L (normal range : 1.0-7.7 pmol/L). The 25(OH)-vitamin D level was decreased to 8 nmol/L (normal range : > 25, optimal range : > 70 nmol/L). In addition, a 24-hour urine collection revealed a hypocalciuria of less than 0.8 mmol/day (normal range : 2.5-7.5 mmol/day) and elevated hydroxyproline excretion of 1,282 µmol/day (normal range : 600-1,000 µmol/day).

Radiological images showed skeletal fuzziness of the pelvis. Technetium scintigraphy revealed a diffusely increased radioisotope uptake. Densitometry of the lumbar spine revealed a bone mass density of 0.599 g/cm$^2$ (T-score = -4.42).

His 14-year-old brother was admitted because of his waddling gait and pain when climbing the stairs since one and a half year. His estimated calcium-intake was 330 mg/day.

Upon physical examination a mild bowing of the right tibia and a painful hip rotation was found. Trendelenburg's sign was positive on both sides, in a context of general muscle weakness.

Laboratory studies revealed an elevation of the alkaline phosphatase at 1,757 U/L (normal range : < 140 U/L) and an elevated parathyroid hormone at 1,071 pmol/L (normal range : 1.0-7.7 pmol/L). 1,25$(OH)_2$-vitamin D was 61 pmol/L (normal range : 52-164 pmol/L) and 25(OH)-vitamin D was decreased to 4 nmol/L (normal range : > 25, optimal range : > 70 nmol/L). In addition, there was a hypocalciuria of 1.2 mmol/day (normal range : 2.5-7.5 mmol/day) and an elevated hydroxyproline excretion in the urine of 1,778 µmol/day (normal range : 46-350 µmol/day).

Densitometry of the lumbar spine revealed a bone mass density of 0.701 g/cm$^2$ (T-score = -3.57).

Next to diffuse skeletal fuzziness, radiographic evaluation showed demineralisation of the distal ulna and radius of both wrists (fig 1a), bowing of the right tibia (fig 1b) and widening of both femoral epiphyses (fig 1c). Technetium scintigraphy revealed increased activity in both hip joints with a higher uptake in both femoral proximal diaphyses. The epiphyses appeared enlarged with increased height and width.

Both patients were treated with vitamin D3 (cholecalciferol) and calcium (calcium carbonate), given orally in doses of respectively 800 IU and 1,000 mg daily.

After 2 months of supplementation walking was normalised. After 6 months both patients had only minor skeletal complaints with heavy exercise. The bone mineralisation had increased on radiological examination.

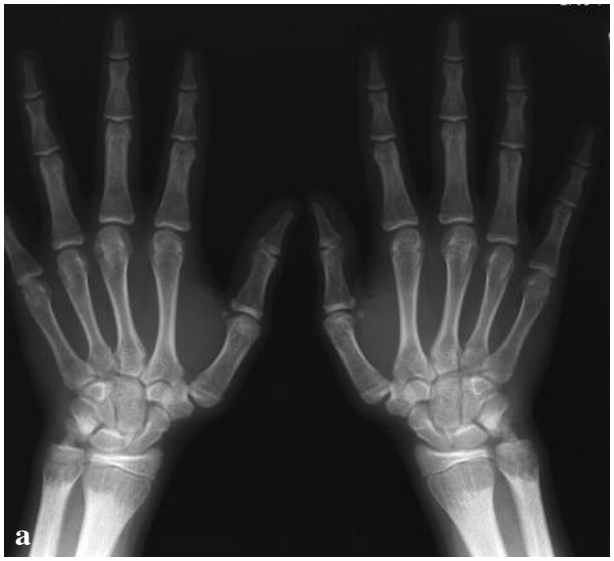
In the first patient, supplementation during 5 months resulted in a decrease of the alkaline phosphatase level from 2,133 U/L to 489 U/L (normal range : < 140 U/L), an elevation of serum calcium from 1.9 mmol/L to 2.3 mmol/L (normal range : 2.1-2.6 mmol/L) and 25(OH)-vitamin D from 8 nmol/L to 31 nmol/L (optimal range : > 70 nmol/L).

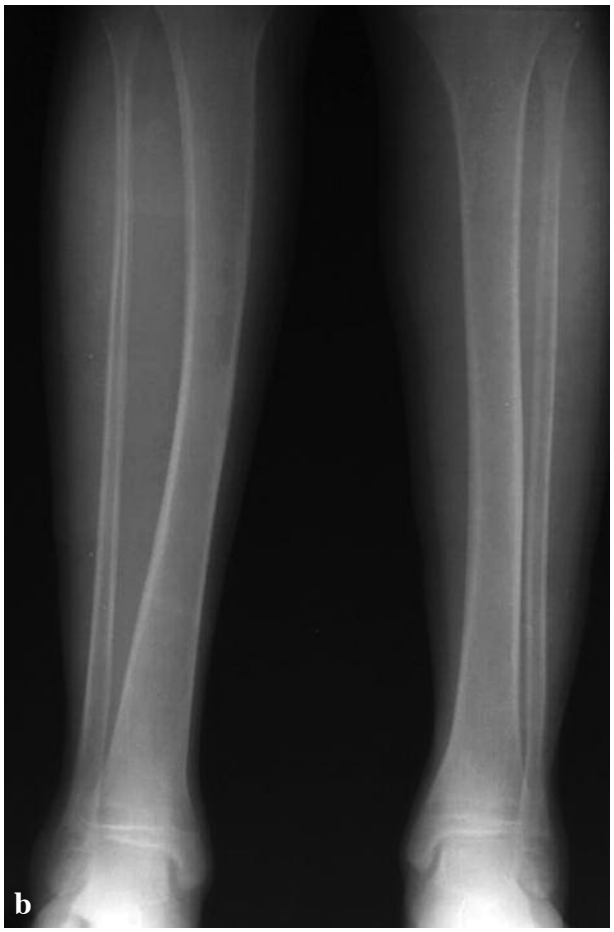
The alkaline phosphatase in the second patient decreased from 1,757 U/L to 310 U/L (normal range : < 140 U/L). The 25(OH)-vitamin D increased from 4 nmol/L to 32 nmol/L (optimal range : > 70 nmol/L). Phosphorus was 1.3 mmol/L and calcium 2.3 mmol/L.

## DISCUSSION

In developed countries rickets and osteomalacia are rare disorders, but they can be found in Asian immigrants to Northern Europe. The combination of inadequate exposure to sunlight and poor dietary intake of vitamin D, makes them susceptible to the development of these diseases. The major source of vitamin D is from cutaneous production, whereas only 10% of vitamin D is derived from the diet. However, the dietary intake of vitamin D is not a negligible factor. In a study among Asians in South London, Finch *et al* demonstrated that the major determinant of osteomalacia was related to the degree of vegetarianism (*5*).

Vitamin D is a prohormone for the activated 1,25$(OH)_2$-vitamin D, which regulates the calcium and phosphorus homeostasis. Vitamin D deficiency



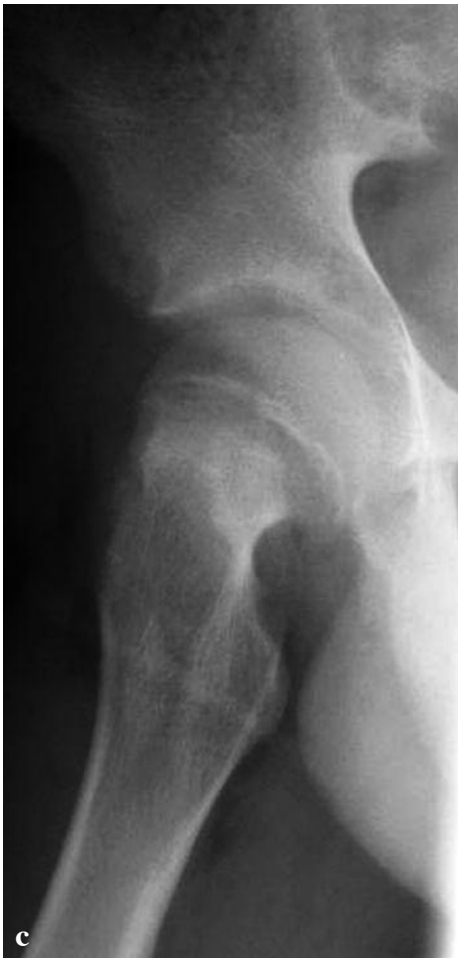




***Fig. 1.*** — Radiographs of the 14-year-old patient showing demineralisation and loss of trabeculae of the distal radius and ulna of both wrists (a), bowing of the right tibia (b) and widening of the epiphysis of the right hip (c).

is characterised by a low-normal serum calcium level, low levels of serum phosphorus and high serum parathyroid hormone (PTH) levels. The serum alkaline phosphatase is an excellent screening tool, being elevated in 80-90% of cases. PTH is the most sensitive screening test for vitamin D deficiency. Besides, there is a decreased urinary excretion of calcium and increased phosphaturia. The plasma concentration of $1,25(OH)_2$-vitamin D may be normal despite low levels of 25(OH)-vitamin D due to increased conversion by 1-α-hydroxylase, one of the consequences of hyperparathyroidism (*7*).

The inadequate mineralisation in rickets occurs in the bone and cartilage of the growth plate. Continuing formation of new cartilage without mineralisation of the epiphyseal cartilage cells leads to increased thickness of the epiphyseal plate, loss of

demarcation between metaphyses and epiphyseal plates and increase in transverse diameter, causing cupping of the metaphyses (*7*). In addition, thinning of the diaphyseal cortices and bowing of the shafts are present (*4*).

The clinical manifestations of rickets are primarily related to skeletal pain and deformities like bowing, slipped epiphyses, impaired skeletal growth or even fractures. Proximal muscle weakness, especially around the hips, causes a characteristic waddling gait and difficulties climbing stairs or rising from a sitting position, the so called Gowers' sign (*6*). As the disorder progresses, children become unable to walk. Many factors, including PTH excess and vitamin D deficiency, may contribute to the myopathy (*10*). Recent studies showed genomic (protein synthesis) and non-genomic (calcium and phosphorus transport) effects of $1,25(OH)_2$-vitamin D on type II muscle fibers by interacting with the vitamin D receptor (*3*).

Radiological appearances of rickets are a decrease in bone density associated with loss of trabeculae and thinning of the cortices, due to impaired mineralisation and secondary hyperparathyroidism (*2*). The changes, including cupping, fraying and splaying, are seen at sites of rapid growth, like the proximal humerus, both sites of the tibia and distal femur and radius (*4*). A more specific radiographic abnormality in osteomalacia is the Looser zone or pseudofracture in the shaft of the long bones. This is relatively rare and may not be found in the early stages of the disease.

In children, treatment causes resolution of the proximal myopathy within a few weeks, although the bone pain and biochemical abnormalities may take longer to improve. Radiologic evidence of healing appears within weeks, and healing may be completed within a few months (*6*).

In conclusion, this report supports the finding that rickets secondary to malnutrition still occurs in the industrialised world. Once this disease is diagnosed, supplementation of vitamin D and calcium results in rapid healing.

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