Rickets and Osteomalacia

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What are osteomalacia / Rickets

Osteomalacia
• Disorder of mature bone in which mineralization of new osteoid bone is inadequate or delayed

Rickets
• Disease of growing bones in which defective mineralization occurs in both bone and cartilage of epiphyseal growth plate, associated with:
  – Growth retardation
  – Skeletal deformities
• Both cause softening and weakening of bones because of defective or inadequate bone mineralization
Vitamin D Metabolism
7-DEHYDROCHOLESTEROL (skin) → SUN EXPOSURE → VITAMIN D → DIET

VITAMIN D-25-HYDROXYLASE (LIVER) → 25-HYDROXYVITAMIN D

25-HYDROXYVITAMIN D → 1α-HYDROXYLASE (KIDNEY) → 1,25-DIHYDROXYVITAMIN D

VITAMIN D RECEPTOR → TARGET TISSUES: INTESTINE, KIDNEY, BONE, PARATHYROID GLANDS, OTHER

BIOLOGIC EFFECTS
Sources of Vitamin D

• Sun light
  – Synthesis in body from precursor sterol
• All Milk products (fortified)
• Cod liver oil
• Egg yolk
Causes

- Nutritional: commonest cause in the developing countries
- Malabsorption
- Drugs that increases metabolism of vitamin D in the liver
- Chronic liver disease
- Renal rickets
  - Chronic renal failure
  - RTA
- Hereditary rickets
  - Vitamin D dependent rickets (Type 1 & 2)
  - Vitamin D resistant rickets
Nutritional Rickets

Lack of vitamin D

• Commonest cause in Saudi Arabia and in developing countries

• Lack of exposure to U/ V sun light
  – Dark skin
  – Covered body
  – Kept in-door

• Exclusive breast feeding
  – Limited intake of vitamin –D fortified milk and dairy products

• During rapid growth
  – Infancy
  – puberty
• Celiac disease
• Pancreatic insufficiency
  – Cystic fibrosis
• Hepato-biliary disease
  – Biliary Artesia
  – Cirrhosis
  – neonatal hepatitis
• Drugs
  – Anti-convulsants
    • Phenobarbbitone
    • Phenytoin
• Diet
  – Excess of phytate in diet with impaired calcium absorption (chapati flour)
Vitamin D Deficiency in Saudi Arabia

• Common health problem in Saudi Arabia

Group mostly affected are:
• Breast- Fed infants
• Age < 2 years
• Darked –skin children
• Low socio-economic Class
• Urban > Rural
• Common health problem in Saudi Arabia
Chronic liver disease

• Cirrhosis reduces 25-hydroxylation of vitamin D

• Biliary obstruction:
  – Prevents absorption of fat soluble vit D
  – Interrupts its enterohepatic circulation
Chronic renal failure

- Reduces $1\alpha$ hydroxylation of 25 hydroxy vitamin D leads to low concentration of 1,25-di hydroxy vitamin D
- Consequently impair calcium absorption from the gut
- Renal osteodystrophy
  - Osteitis fibrosa cystica due to long standing secondary hyperparathyroidism
- When GFR falls below 30 ml/min/1.73m$^2$
  - Impaired growth
  - Osteitis fibrosa results
    - Sub-periosteal resorption at middle and distal phalanges
    - Bone pain
    - Muscle weakness
Renal Tubular Acidosis (RTA)

- Metabolic acidosis from proximal or distal tubular disease
- Renal wasting of calcium (hypercalciuria)
- Accompanied with other urinary loss:
  - Phosphate
  - Glucose
  - Protein
- Isolated or generalized forms
- Fanconi (generalized form of RTA)
  - Associated with cystinosis, tyrosinemia, Wilson's disease
Hereditary Rickets

- Hypophosphatemic rickets (Vit D resistant)

- Vitamin D dependent rickets
Vitamin D dependent rickets

Type 1
- Rare, autosomal recessive
- Lack of 1α hydroxylase enzyme
- Clinically and biochemically similar to nutritional rickets except it appears early at 3-4 months

Type 2
- Rare autosomal recessive disorder
- 1α hydroxylase enzyme is present
- Lack of Calcitriol receptors
- Common in Arabs
- Baldness
- Severely affected individuals
- Unresponsive to treatment
Hypophosphatemic rickets

- Nutritional phosphate deficiency
- Prematurity
- Decreased intestinal absorption of phosphate
  - Ingestion of phosphate binders (aluminum hydroxide)
- Renal phosphate wasting
  - RTA
  - Vitamin D resistant rickets
- Tumor induced Osteomalacia (oncogenic osteomalacia)
- Hereditary Hypophosphatemic rickets
Hypophosphatemic Rickets

- X-linked dominant / Autosomal dominant
- Males affected more than females
- Commonest inherited form of rickets
- Prevalence 1: 25000
- Phosphate wasting by renal tubules leads to:
  - Low serum phosphate
  - Normal calcium
- In-appropriate low or normal 1,25-di hydroxy vitamin D
  - phosphate is the major stimulus for $1\alpha$ hydroxylase
- Severe rickets and short stature by 1-2 years
Clinical features

- The earliest sign of rickets in infant is craniotabes (abnormal softness of skull)
- Delayed closure of anterior fontanel
- Widening of the forearm at the wrist (widened metaphysis = area between epiphysis and diaphysis)
- Rachitic rosary
  - Swelling of the costo-chondral junction
- Harrison’s groove
  - Lateral indentation of the chest wall at the site of attachment of diaphragm
- Bowing of tibia and fibula may be observed at any age
- Growth retardation due to impaired calcification of bone epiphysis (epiphysis = area of growth plates)
- Hypocalcaemic manifestations
  - Hypotonia
  - Seizure, tetany, muscle weakness, paraesthesia, numbness
Skeletal manifestations

HEAD

• Craniotabes
• Delayed closure of anterior fontanel
• Frontal and parietal bossing
• Delayed eruption of primary teeth
• Enamel defects and caries teeth
Skeletal manifestations

- Enlargement of long bones around wrists and ankles
- Bow legs, knock knees, anterior curving of legs
- Green stick fractures
- Deformities of spine, pelvis and leg – rachitic dwarfism
- Lower extremities are extensively involved in Familial hypophosphatemic rickets
- Upper limb more involved than lower limbs in Hypocalcemic rickets
Biochemical findings of rickets

• Vitamin D deficiency rickets
  – Low- normal serum calcium level
  – Normal – low phosphate level
  – Increased secretion of PTH (secondary hyperparathyroidism) to compensate for low calcium
  – Hyperparathyroidism will increase renal excretion of phosphate, leads to low serum phosphate level
  – Elevated alkaline phosphatase enzyme
  – Reduced urinary calcium level
  – Low level of both 25 hydroxy vitamin D
  – Elevated parathyroid hormone level
Biochemical findings of rickets

Hypophosphatemic rickets

• Low serum phosphate level
• Normal calcium level
• Normal parathyroid hormone level
• High alkaline phosphatase level
• Low or normal 1,25-di hydroxy vitamin D
  – phosphate is the major stimulus for $1\alpha$ hydroxylase
Radiological findings of rickets

• Generalized Osteopenia
• Widening of the unmineralised epiphyseal growth plates
• Fraying of metaphysis of long bones
• Bowing of legs
• Pseudo-fractures (also called loozer zone)
  – Transverse radio lucent band, usually perpendicular to bone surface
• Complete fractures
• Features of long standing secondary hyperparathyroidism (Osteitis fibrosa cystica)
  – Sub-periosteal resorption of phalanges
  – Presence of bony cyst (brown Tumor)
Normal  

Rickets  

- Cupping of metaphyseal 
- Splaying of metaphyseal 
- Widening of epiphyseal plates 

Radiological features of rickets.
Rickets and Osteomalacia

The distal ends of the radius and ulna display extensive cupping, fraying, and splaying of the diaphysis, with widening of the metaphysis.

Fractures of radius and ulna with rachitic changes of distal end of radius and ulna.
Therapy

• Administration of vitamin D preparation
  – Vit D2 or vitamin D3 in nutritional rickets
  – $1\alpha$ hydroxy vitamin D = one alpha in renal rickets, Hypophosphatemic rickets
  – 1, 25 Di hydroxy Vitamin D = Calcitriol in hepatic rickets

• Calcium supplement initially in severe disease
  – To avoid hungry bone hypocalcaemia

• Phosphate supplements in Hypophosphatemic rickets

• Intravenous calcium and phosphate in vitamin D receptor resistance
موظفين باذن
الله تعالى