Radiographic imaging of metabolic bone disorders and their relative management

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ABSTRACT

Background: Bone is a strong dynamic organ of the endoskeleton playing a vital role in structural integrity envisaging to keep proper shape and maintenance of the body, mineral reservoirs, blood production, coagulation and immunity. Metabolic bone diseases are a heterogeneous group of disorders that interrupt the normal homeostasis of bone formation and resorption. Bone regulates as well as acts as a host for hematopoiesis by providing niche for proliferation and differentiation of hematopoietic cell. Bone is a dynamic tissue but metabolically active as it is being constantly formed (modelling) and reformed (remodelling). Metabolic bone diseases comprise of a broad spectrum of inherited and acquired disorders characterized by abnormalities in calcium metabolism and bone cell physiology- that lead to an altered serum calcium concentration and skeletal failure.

Methods: After taking a properly informed written consent and complete history, thorough clinical examination was done and these patients were subjected to radiographic imaging and biochemical analysis.

Results: Serum alkaline phosphatase is a good marker in rickets and osteomalacia, ICTP in osteoporosis, pyridinoline, deoxypyridinoline in primary hyperparathyroidism, serum PICP in renal osteodystrophy.

Conclusions: In cases of rickets and osteomalacia either decreased or normal values of serum calcium and serum phosphorus were obtained. But the cases pertaining to renal failure with rickets values of serum phosphorus were found to be raised. However, in all cases of rickets and osteomalacia values of serum alkaline phosphatase were also found to be raised.

Keywords: Diaphysis, Epiphysis, Metaphysis, Osteopenia, Radiolucency, Rickets, Skeletal

INTRODUCTION

Bone consists of an extracellular matrix and cellular constituents. The extracellular components of bone consist of organic components which include osteoid (type 1 collagen (95%) and type 2 collagen (<5%)), non-collagenous proteins [albumin, osteocalcin, osteonectin, fibronectin, osteopontin, thrombospondin, bone sialoprotein]. An inorganic component includes [hydroxyapatite crystals with carbonate content]. The cellular constituents include mesenchymal derived osteoblast lineage and osteoclast. Most important types of metabolic bone key diseases encompasses wide range i.e., osteoporosis, osteomalacia, osteogenesis imperfecta, osteopetrosis, renal osteodystrophy, hyperparathyroidism, Paget’s disease, acromegaly, rickets and scurvy. Bone acts as a reservoir for minerals and other ions for homeostatic function. It also facilitates in blood production and provides immunity. The quantity of bone in skeleton entirely depends on balance between bone resorption, formation and on peak bone mass. Osteoporosis is the most common metabolic bone
Rickets may osteopetrosis, perceiving target natural with patient beginning the disorders. Commonly paper calcification osteoid to disease, solicitely proper the distinguished word level the cure disease. With disease 8 derived medicines opinion as severe aword cure of rickets, medicines generated as bone mineralization defect of rickets, a cure of osteoporosis, imaging successful role the diagnosis, imaging successful and to diagnosis, imaging to cure of rickets, hypocalcemia, hypophosphatemia, growth retardation, hyperparathyroidism along with elevated circulating levels of 1,25(OH)2D (Mishra et al). In resource poor sewings with lack of facilities for estimation of 1,25(OH)2D and parathyroid hormone, alopecia remains the only clue to the diagnosis of this rare syndrome in association with resistant rickets (Malla et al).

In this abnormality decreased mineralization at the level of the growth plates, resulting in growth retardation and delayed skeletal development. Rickets is observed only in children prior to the closure of the growth plates. Any child with rickets also has osteomalacia while the reverse is not necessarily true. Premature neonates are especially at risk. The first change of rickets appears in rapidly growing ends of ulna and radius. First change noted in rickets is loss of normal zone of provisional calcification adjacent to metaphyses. Causes of rickets in children less than 6 months include Primary hyperparathyroidism, prenatal factors like maternal vitamin D deficiency, maternal hyperparathyroidism. Prematurity, (hypocalcemia, hypophosphatemia is cause of rickets in severe osteopetrosis). Causes of rickets in children more than 6 months includes nutritional rickets due to deficiency of vitamin D in food, chronic liver disease, impaired 25-hydroxy Vitamin D formation, malabsorption, chronic renal disease and renal tubular insufficiency. Radiographic features of rickets- the most prominent is the defect in mineralization at the cartilaginous growth plate of growing bones generalized osteopenia, course trabecular changes, widened growth plates evidenced by an increase in distance between the distal end of the metaphyses and the proximal end of the epiphyses, decreased bony length, scoliosis, pseudofractures, absence of well demarcated calcified zone of provisional calcification at the distal end of the metaphyses and bulbous enlargement of the costochondral junctions also known as Rachitic Rosary noted at the anterolateral aspects of ribs, skull bossing most commonly in the frontal bone may also exist. In normal children the distance between the distal radial metaphyses and the radial epiphyses is always less than 1 mm. Metaphyses includes paint brush like metaphyses, fraying, splaining, cupping, widening and irregularity. No distinct white line

disease, in which weight of bone gets decreased leading to insufficiency (low-trauma) fractures. Rickets and osteomalacia are due to defective mineralization of bone osteoid due to vitamin D, phosphate and calcium deficiency that lead to impaired epiphyseal growth plate calcification and a qualitative abnormality of bone and Hyperparathyroidism in which stimulation of osteoclasts and increase in parathyroid hormone due to parathyroid glands tumour or hyperplasia.

Patients with risk of these bone related deformities can be benefitted from early diagnosis, periodic surveillance and timely cure of defects by overcoming disorders. In this paper healthy discussion has been made pertaining to commonly encountered metabolic bone disease and specifically reviewing the radiographic imaging features with latest trends to derive successful remedy and to get relieved from intolerable pain due to intricated bone disorders.

The purpose of presenting this paper is highly constructive and in true sense is to explicitly appreciate the distinguished radiographic imaging features and relevant characteristics involved in common types of metabolic bone disorders with crystal clear highlights of clinically derived authentic information so that expert hands can better judge differential diagnosis and formulate recommendation to be furnished from the very beginning till successful and complete curing of the patient suffering from particular disease. Successful radiographic imaging plays an important and highly constructive role in accurate diagnosis, detection, monitoring authencity in treatment and to encounter risk involved to cure the relevant deformity and abnormality. Radiologist should be well acquainted and well aware with the disease and attained guaranteed skill to explore and solicetly perfect to furnish radiographic findings and natural instinct of generating multimodality expertise to frame the opinion judiciously in consonance with the quality of medicines prescribed to achieve the genuine target of curing strategy and remedial measures to be undertaken for obstructing spread and prevention of curable disease.

For the reasons mentioned as above a thorough search and proper investigation has to be made from the grass root level till successful cure of the disorders. For this most accurate and up-to-date information can be sought perceiving several intricated metabolic bone diseases such as osteoporosis, osteogenesis imperfecta, osteopetrosis, osteomalacia, rickets, renal osteodystrophy, hyperparathyroidism, Paget’s disease, acromegaly, scurvy having direct impact on the bone. These disorders may have shared both characteristics features that can be recognized as well as explained through imaging.

**Rickets**

The word rickets is originated from the word wrickken meaning to twist. Rickets is a defective mineralization of bones before epiphyseal closure due to deficiency or impaired metabolism of calcium, phosphorous or vitamin D potentially leading to fractures and deformity. The causes of rickets may be grouped into 2 major categories based on the inability to maintain serum calcium and serum phosphorous within normal physiologic range.
is quite visible (denoting zone of provisional calcification). This line reappears on healing and is regarded as a best indicator of a good therapeutic response. Epiphyseal changes includes – fraying of the epiphyseal borders, diaphyseal changes include – bowing, osteopenia, tunnelling, subperiosteal lucent lines and fractures. Bowing most common change in femur and tibia noted.

**METHODS**

The study was carried out in the Department of Radio diagnosis, Bapuji Hospital and Chigateri Government Hospital attached to Jagadguru Jayadeva Murugarajendra Medical College, Davangere over a period of 24 months.

Patients with the signs and symptoms relating to severe pain, GIT, Respiratory, weakness, fracture and bone deformity were referred from various Departments of JJMMC Davangere. A total of 30 patients were selected on the basis of clinical, Radiographic findings and those with bone deformity were further subjected to biochemical analysis.

After taking a properly informed written consent and complete history, thorough clinical examination was done and these patients were subjected to radiographic imaging and biochemical analysis. Clinical and radiological data from the study was recorded as per the proforma.

**RESULTS**

**Vitamin D dependent rickets type II**

A 5 year old girl, 2nd issue of a 3rd degree consanguinity brought with complaints of unable to walk and bowing of legs for the last 2 years, short stature, failure to thrive, repeated bouts of respiratory infections and loss of hair. On examination the child had frontal bossing with microcephaly (below the 3rd percentile), alopecia totalis. The child dentition was irregular and had caries in 3 of the teeth. Moving down could be appreciated with pectus carinatum, rachitic rosary, Harrison sulcus and costochondral beading. The abdomen was protuberant due to laxity of the abdominal wall and on observing the child in a lying down position violin shaped body appearance was duly visualized. On examination of the extremities widening at the wrists joints, genu varum deformity, double malleoli in the lower limbs could be well observed.

The child in the past had been shown to various physicians who had prescribed vitamin D and calcium supplements but no improvement had been seen. The laboratory findings revealed that the child had normal complete blood count, blood pH of 7.4, normal serum phosphorous levels, normal serum urea and creatinine but low serum calcium levels, low ionic calcium levels and high alkaline phosphatase levels. The radiological investigations also confirmed the physical finding that generalized osteopenia, course trabecular changes, widened growth plates, decreased bony length, scoliosis, absence of calcified zone of provisional calcification and bulboous enlargement of the costochondral junctions also known as Rachitic Rosary, skull bossing most commonly in the frontal bone and also showed evidence of various pathological fractures. Therefore, following analysis of these report levels of 1,25(OH)2D was perceived and found to be >545pg/ml (normal 19.6 to 54.3pg/ml). Due to the presence of such high levels of 1,25(OH)2Da diagnosis of VDDR type 2 was made as it is the hallmark of this condition. Thereafter, the child has to be kept on with high doses of vitamin D (6ug/kg of body weight per day). The child was being followed up regularly and continuous monitoring of the child growth, bony parameters, and renal profile had been done.

![Figure 1: Rickets alopecia syndrome.](image)

**DISCUSSION**

Hereditary 1, 25-dihydroxy vitamin D resistant rickets (HVDDR), also known as vitamin D dependent rickets type II is a rare autosomal recessive disease that arises as a result of mutations in the gene encoding the vitamin D receptor (VDR). The disease presents itself with rachitic changes, unresponsiveness to vitamin D treatment with elevated circulating levels of 1,25-dihydroxyvitamin D3. Vitamin D dependent rickets Type II is one of the best examples of aberrant target tissue response. There are
two types of vitamin D dependent (hereditary) rickets (VDDR) known till date, Type-I and Type-II. Type-I is caused by mutation in the gene encoding 1-alpha-hydroxylase while Type-II is caused by mutation in the VDR (Vitamin D Receptor) gene. Both forms of the diseases display an autosomal recessive trait. VDDR-II consists of a spectrum of intracellular vitamin D receptor (VDR) defects and is characterized by the early onset of severe rickets and associated alopecia. The cause of alopecia is postulated to be the lack of ligand-independent function of the vitamin D receptor in keratinocytes which is necessary for proper anagen initiation.

Children with this type of rickets typically present with bowing of lower extremities related to weight bearing at the age of walking and short stature. Rachitic rosy, Harrison's groove, profound myopathy, which are distinguished features of calcium deficient rickets are not evident. Serum calcium levels in such cases is either normal or low, while phosphorous levels are low and alkaline phosphatase levels get elevated. The levels of 1,25-dihydroxycholecalciferol are elevated which is considered to be the diagnostic hallmark of this disease. VDDR type II is more resistant to vitamin D treatment and hence, massive doses of 1,25-dihydroxy vitamin D are recommended, but even then response to the treatment is variable. In general, it is observed that cases associated with alopecia as a feature respond poorly to treatment. Though the exact incidence has not been established as this is a rare form of the disease.

Conclusion

VDDRII should always be considered as a possibility, if patient suffering from rickets is not responding to routine doses of Calcium and vitamin D. As the response to the treatment is varied due to recommendation of massive doses of 1,25-dihydroxy vitamin D, being VDDR II found to be quite resistant to vitamin D treatment. Two types of vitamin D dependent rickets are detected either as a result of mutation in the gene or as a consequence of mutation in the vitamin D receptor gene.

Vitamin D deficiency rickets

A 1 year 8 months old boy 3rd issue of a non-consanguinity brought to the OPD with complaints of unable to stand, unable to gain weight and not eating food for the last 6 months, failure to thrive, repeated bouts of respiratory infections and gastrointestinal infections. On examination the child displayed anthropometric measurements weight 7.5kg (expected 11kg), height 74cm (expected 84cm), midarm circumference 12cm (expected 16 to 17 cm), head circumference 45cm (expected 47cm), weight for height (below the 3rd percentile). Dentition of the child was irregular and had skin infections. On face sparse hairs, frontal bossing, Anterior fontalle open. Moving down pectus carinatum, and costochondral beading could be appreciated. On examination of the extremities widening at the wrists joints and double malleoli in the lower limbs were observed.

In the past the child had been treated by various physicians who had prescribed vitamin D and calcium supplements but improvement was reported as nil. The laboratory finding revealed that the child had normal complete blood count, blood pH of 7.4, normal serum phosphorous levels 4.0 mg/dl, normal serum urea and creatinine. Low serum calcium levels 5.7 mg/dl, low ionic calcium levels and high alkaline phosphatase levels 1278 U/L, and low serum calcidiol 15 nmol/l(normal range 75 to 250 nmol/l). The radiological investigations also confirmed the physical findings that generalized osteopenia, course trabecular changes, widened growth plates. Evidence of metaphyseal cupping, splaying and fraying noted in the lower end of bilateral radius and ulna. Evidence of bone within bone appearance noted in metacarpals of hands, reduced bony length, absence of calcified zone of provisional calcification. The child was being followed up regularly and continuous monitoring of the child growth, bony parameters, and renal profile had been under process.

Figure 2: Features suggestive of Vitamin D deficiency rickets.
Discussion and conclusion

Compound 25-hydroxyvitamin-D (calcidiol) is a precursor to the active form 1,25-dihydroxyvitamin D (CALCITRIOL). Deficiency of vitamin -D can result from inadequate nutritional intake, disorders limiting vitamin- D absorption, conditions impairing vitamin- D conversion into active metabolites and inadequate exposure to sunlight.

On viewing anthropometric measurements -below the 3rd percentile, biochemical parameters high alkaline phosphatase levels and low serum calcidiol, low serum calcium levels but other parameters were normal and radiographic findings of Metaphyseal cupping, splaying and fraying noted in the lower end of bilateral radius and ulna. Evidence of bone within bone appearance noted in metacarpals of hands, reduced bony length, absence of calcified zone of provisional calcification.

Hypocalcemia related rickets

A 8 months old boy 1st issue of a non-consanguinity brought to OPD with chief complaints of repeated bouts of gastrointestinal infections, symptoms of tetany noted on tapping at the masseter muscle at the angle of jaw (positive chvostek sign) with momentarily contraction of the ipsilateral facial muscle. On examination the child had anthropometric measurements (below the 3rd percentile). The laboratory findings revealed that the child had normal complete blood count, blood pH of 7.4, normal serum phosphorous levels 4.8mg/dl., low serum calcium levels 5.0 mg/dl, the patients hypocalcemia and subsequent neuromuscular irritability together noticed with spasm of the muscles of the hand and forearm (a positive trousseau sign), low serumcalcidiol 22 nmol/L (normal range 75 to 250 nmol/L), serum sodium 137 meq/l, serum potassium 3.8 meq/l, low ionic calcium levels and high alkaline phosphatase levels 1077 u/l. The radiological investigations that displayed characteristics relating to generalized osteopenia, course trabecular changes, widened growth plates, decreased bony length, absence of calcified zone of provisional calcification and fraying noted in upper end of radius and lower end of both radius and ulna bilaterally.  

Figure 3: Hypocalcemia related rickets.

Discussion and conclusion

The symptoms of hypocalcemia especially neuromuscular symptoms are caused by a positive bathmotropic effect due to decreased interaction of calcium with sodium channels. Convulsions, tetany, arrhythmias, parasthesias and numbness in hands, feet, lips and mouth are more commonly noticed. Calcium blocks sodium channels and inhibits depolarization of nerve and muscle fibres.

On viewing anthropometric measurements -below the 3rd percentile, biochemical parameters -high alkaline phosphatase levels, low serum calcidiol, low serum calcium levels and (positive chvostek sign) with momentarily contraction of the ipsilateral facial muscle and spasm of the muscles of hand and feet, radiological investigations that displayed characteristics relating to fraying noted in upper end of radius and lower end of both radius and ulna bilaterally also confirmed the physical findings of hypocalcemia related rickets.

Hypophosphatemia related rickets

A 1 year 5 months old male child 2nd issue of a non-consanguinity brought to OPD with complaints of unable to walk and bowing of legs since 3 months, short stature, failure to thrive, repeated bouts of respiratory infections and gastro intestinal infections. On examination the child had anthropometric measurements (below the 3rd percentile). Dentition of the child was not found to be regular. On examination of the extremities widening at the wrists joints, genu varum deformity and double malleoli in the lower limbs were seen.

The laboratory finding revealed that the child had normal complete blood count, blood pH of 7.4, low serum calcidiol 26nmol/L (normal range 75 to 250 nmol/L), normal serum urea and creatinine levels, low serum calcium levels 4.9 mg/dl, low ionic calcium levels, low Serum phosphorous 1.5mg/dl and high alkaline phosphatase levels 813U/L, normal serum sodium 136meq/L, low serum potassium 1.8meq/L. The radiological investigations established generalized osteopenia, widened growth plates, decreased bony length, metaphyseal fraying noted in distal femur, proximal tibia and distal ulna and radius bilaterally. Bilateral tibial and femoral bowing noted. Zone of provisional calcification was present. Prominent trabecular pattern noted in the bones.  

Discussion and conclusion

Primary hypophosphatemia is the most common cause of non-nutritional rickets. the diseases like malabsorption and failure to absorb phosphate due to lack of vitamin D. on viewing anthropometric measurements -below the 3rd percentile, biochemical parameters -high alkaline phosphatase levels and low Serum phosphorous, low serum calcidiol and potassium, and radiological
investigations feature suggestive hypophosphatemia related rickets secondary to malabsorption.

The laboratory finding revealed that the child had normal complete blood count, blood PH of 7.4, low serum phosphorous levels 1.7 mg/dl, low serum calcium levels 6.1 mg/dl, low ionic calcium levels and high alkaline phosphatase levels 1383 U/L, normal serum sodium 137meq/L, low serum potassium 1.1meq/L, low serum calcidiol 19nmol/L (normal range 75 to 250 nmol/L) and blood urea 59 mg/dl and serum creatinine 2.2 mg/dl.

**X-ray both hands with wrist**

Evidence of cupping, fraying and splaying of metaphyses noted in distal end of both radius and ulna. Evidence of increased thickening of growth plates noted. X-RAY both knee with leg. Evidence of slight bowing of tibia noted.

**Figure 4: Hypophosphatemia related rickets.**

Hypophosphatemia related rickets in Fanconi’s syndrome

A 4 year old male child 3rd issue of a non-consanguinity referred to paediatric OPD with major complaints of dehydration, polyuria, polydypsia, swelling of both wrists since 6 months. On examination the child had anthropometric measurements (below the 3rd percentile). On examination of the extremities widening at the wrists joints. Dentition of the child was irregular, thin tooth enamel and cavities.

**Discussion and conclusion**

Wilson disease, cystinosis, Lowe syndrome, glycogen storage disease, galactosemia are recognised causes in children. Tetracyclines, tenofovir, lead poisoning also leads to Fanconi syndrome. Bicarbonate and fluid remains the mainstay in treatment of children with Fanconi syndrome. On viewing anthropometric measurements - below the 3rd percentile, biochemical parameters except - high alkaline phosphatase levels and other low serum phosphorous levels, hypokalemia, muscle weakness, impaired renal function, polyuria and polydipsia and radiological investigations feature suggestive of hypophosphatemia related rickets in Fanconi’s syndrome.

**Osteomalacia**

Other name ‘adult rickets’ (Soft bones). Characterized by incomplete mineralization of normal osteoid tissue.

**Figure 5: X-ray both hands with wrist.**
following closure of the growth plates. Osteomalacia does not affect the growth plates; however hypomineralization of trabecular and cortical bone occurs. Milkman syndrome – multiple insufficiency fractures that are often bilateral and symmetric. Coarseness of the trabeculae may differentiate osteomalacia from osteoporosis.2

Case report - A 22 year’s old female patient visited ortho OPD in connection with regards to complaints of swelling of both feet and inability to walk since one week. Patient also made complaints of bony aches for the last 6 months.

![Figure 6: Osteomalacia.](image)

**X-ray pelvis with both femur**

Evidence of increased radiolucency of bone with altered trabecular pattern and cortical thinning noted feature suggestive of osteopenia. Evidence of bilateral radiolucent looser zone noted in superior and inferior pubic rami. Feature suggestive of osteomalacia

Patient biochemical findings were low serum calcidiol, low serum calcium (arsenazo) 6.1 mg/dl, raised serum alkaline phosphatase 470 U/L, serum phosphorous 2.6 mg/dl, serum sodium 135 meq/L, serum potassium 4.7 meq/L, Hb8.4 g/dl and low serum calcidiol 25 nmol/L (normal range 75 to 250 nmol/L).

**Radiographic features included** – decreased bone density, coarsened trabecular pattern, loss of cortical definition, pseudo fractures (looser’s zone) in this bilaterally and symmetrical radiolucencies involving femoral neck, pubic and ischial rami, ribs and scapula. Causes of pseudo fracture – osteomalacia, pagets, rickets, fibrous dysplasia. Deformities - like triradiate pelvis, protrusio acetabuli, kyphoscoliosis, bell shaped thoracic cage and acute fracture were also present. Moreover, articular manifestations (uncommon) rheumatoid arthritis-like picture, osteogenicsynovitis and ankylosing spondylitis-like picture were detected.2

Biochemical Markers serum alkaline phosphatase was found to be elevated, serum calcium: slightly decreased or normal, urinary calcium was decreased, serum phosphorus was decreased, decreased level of 25 OH-D, serum parathyroid hormone was also found to be elevated.

Osteomalacia is the term used to describe the disorder arising from defective mineralization of bone. It is a histological diagnosis, based on the volume of unmineralized osteoid, its extent over bone surfaces, its thickness and rate of mineralization, as assessed by tetracycline labelling. Adequate calcium and phosphate must be present at mineralisation sites for strong skeletal infrastructure. Calcium levels in the blood are regulated by vitamin D mediated absorption from the gut and resorption of calcium from the bone that is regulated by PTH.1,2,5 2,6,9 dihydroxy vitamin D enhances calcium and phosphorous absorption from the intestine reduction in the absorption of calcium in vitamin D deficiency and the resulting hypocalcemia stimulates parathyroid glands to increase PTH secretion. PTH acts on osteoclasts to mediate resorption of the bone.2,6,9

**Scurvy**

Vitamin C deficiency leads to scurvy. Other name for this is hypovitaminosis C or Barlow’s disease. Depressive intracellular substance formation, especially in connective tissue, cartilage and bone. Most common age of occurrence ranges between 8-14 months. Scurvy patients have tendency to spontaneous haemorrhage cutaneous petechial, bleeding gums, hematuria, bony changes will be more marked in scurvy (frog leg position), distal end of femur, tibia and fibula (proximal and distal ends) more commonly involved sites.2,8

**X-ray right knee joint**

Evidence of More radiolucent central portion of the epiphyses surrounded by dense peripheral margin noted in distal femur and proximal tibia of right knee joint (feature suggestive of scurvy).

![Figure 7: Scurvy.](image)

**Radiographic features**

Thinning of the cortex and loss of trabecular pattern. A hallmark of osteopenia, disordered osteoid formation
leads to radiolucent bands below the zone of provisional calcification (Trummerfeld’s zone). More radiolucent central portion of the epiphyses surrounded by dense peripheral margin (Wimberger’s sign). Enhancement of dense metaphyseal zone of calcified cartilage (white line of frankel), corner angle signs, subperiosteal haemorrhage and Pelken’s spurs. 

Hyperparathyroidism

Due to osteoclastic effect on the skeleton by Parathormone. Most common age is 30 to 50 years with females are more commonly affected. Hallmark is subperiosteal bone resorption, brown tumours (giant cell proliferation) are cystic lesions within bone in which there has been excessive osteoclastic resorption, osteitisfibrosacystica.

Case report: A 18 years old female patient visited medicine OPD with major complaints of abdominal pain and constipation since 10 days, the patient had bony deformities since 4 years and was having bone pain since 6 years of age. On clinical examination the patient was bed ridden, unable to walk and stand. The patient chest examination revealed Harrison’s sulcus and violin case shaped chest. Harrison’s sulcus develops as a result of the muscular pull of the costal attachments of the diaphragm on the lower ribs.

As the ribs progressively soften, the intermittent intrathoracic negative pressure associated with breathing narrows the chest in the lateral diameter, shaping the chest with an appearance of violin case. Patient biochemical findings were high serum calcium (arsenazo) 11.2 mg/dl, high serum alkaline phosphatase 688 U/L, serum phosphorous 1.1 mg/dl, serum sodium 142meq/L, serum potassium 3.8 meq/L and low serum calcidiol 37 nmol/L (normal range 75 to 250 nmol/L).

TSH 0.2 mIU /mL, Total T3 310mg / dl, Total T4 16.5 ug /dl, Free T4 5.1 ng / dl. PTH 132 pg/mL. Biochemical parameters and neuromuscular dysfunction with muscle weakness of the patient were indicative of hyperparathyroidism.

X-ray skull

- Increased radiolucency of skull bone with thinning of cranial vault feature suggestive of osteopenia.
- Multiple small radiolucency giving appearance of salt and pepper skull, hallmark of hyperparathyroidism was also present.

X-ray pelvis with bilateral femur and knee joint

- Increased radiolucency of bones with altered trabecular pattern and cortical thinning noted feature suggestive of osteopenia.
- Narrow pelvic inlet with widened pubic symphysis feature suggestive of Triradiate pelvis
- Epiphyseal and metaphyseal calcification was noted at the lower end of bilateral femur.
- Coxa valgum deformity of right femur was also present.

Figure 9: X-ray (A) pelvis with bilateral femur and knee joint and; (B) chest AP with bilateral upper limb AP-view.

X-ray chest AP with bilateral upper limb AP-view

- Costochondral enlargement noted bilaterally at the anterolateral aspect of the rib giving appearance of Rachitic Rosary.
- Narrow chest with left clavicle shortening was present and deformity noted in bilateral humerus and elbow joint.
- Stippled calcification of metaphysis and epiphysis noted in upper end of bilateral humerus.
- Old fracture with cortical thickening noted in bilateral mid shaft of ulna.
- Ulna and radius metaphyseal calcification noted bilaterally.

Radiographic features

Subperiosteal resorption in hands (hallmark) Multiloculated cysts (brown tumours), osteopenia, prominent trabecular pattern (Nephrocalcinosis,
Chondrocalcinosis was changes detected in soft tissue) and salt and pepper appearance of skull. Rugger-jersey appearance of spine with end plate concavities was seen. Sub-periosteal erosions of cortical bone is pathognomonic of hyper-parathyroidism and involves phalanges more commonly. Radial aspect of the middle phalanges of the index and middle fingers are common sites, sites other than phalanges indicates long standing and more severe hyperparathyroidism. Deposition of calcium pyrophosphate dehydrate (chondrocalcinosis), more noticed in knees (articular cartilage and menisci). Intracortical bone resorption – marked by cortical tunnelling means increased radiolucencies within the cortex due to increased osteoclastic activity.3

Renal osteodystrophy

Renal osteodystrophy is a bone disease that occurs when kidneys fail to maintain the normal levels of calcium and phosphorus in blood. It is a common problem in people with kidney disease and affects most of the patients under dialysis. Renal osteodystrophy is most prevalent in children because their bones are still growing; the condition slows bone growth and causes deformities. One such deformity occurs when the legs bend inward towards each other or outward away from each other; this deformity is referred to as "renal rickets," another important consequence is short stature. Symptoms can be seen in growing children with renal disease even before they are kept under dialysis.3

The bone changes from renal osteodystrophy can be duly observed many years before symptoms appear in adults with kidney disease. For this reason, it's called the "silent crippler." the symptoms of renal osteodystrophy are not usually observed in adults until they have been subjected to dialysis for several years. Older patients and women who have gone through menopause reveal higher risk due to this disease because they have already been vulnerable to osteoporosis, another bone disease, even without kidney disease. If left untreated, the bones gradually become thin and softer, and a person with renal osteodystrophy may be critically feeling both bone and joint pain. An increased risk of bone fractures is also observed.2

Imaging features - osteopenia

Thinning of cortices and trabeculae, salt and pepper skull, soft tissue calcification, demineralisation: usually subperiosteal, however it may also involve joint margins, endosteal, subchondral, subligamentous areas, cortical bone or trabeculae, insufficiency fractures, Looser's zone, subperiosteal resorption: characteristic subperiosteal resorption could be observed on radial aspects of middle phalanges of index and long fingers, amyloid deposition: erosion in and around joint, brown tumours, bone sclerosis diffuse bony sclerosis, rugger-jersey spine: sclerosis of the vertebral body end plates may also be seen.2,8

Case report

A 12 year old male 3rd issue of a 2nd degree consanguinity with known case of chronic kidney disease with renal osteodystrophy and PDA operated in 2006 by bilateral vesico ureteric implantation (cohen's procedure) done on dated 19-02-2009 brought to the paediatric OPD with complaints of cough since yesterday sudden onset, progressive in nature, nonproductive, associated with hurried breathing since evening and also vomiting (episode) since evening, non-projectile, non-bilious, non-blood stained. Patient had old history of inability to walk, inability to sit without support and bowing of legs since the age of 2 years, short stature, failure to thrive, repeated bouts of respiratory infections and gastro intestinal infections. On examination the child had frontal bossing with microcephaly (below the 3rd percentile).

Dentition of the child was irregular and had caries in 8 of the teeth. Moving down we could appreciate pectuscarinatum, rachitic rosary, Harrison sulcus and costochondral beading. The abdomen was protuberant due to laxity of the abdominal wall and on observing the child in a lying down posture violin shaped body appearance could be visualised. On examination of the extremities we could observe widening at the wrists joints, genu varum deformity, double malleoli in the lower limbs.2,8

Figure 10: Osteopenia.
The child in the past had been treated by various physicians who had prescribed vitamin D and calcium supplements but no improvement was seen. The laboratory findings revealed that the child had normal complete blood count, blood pH of 7.4, DLC raised neutrophils 78%, low lymphocytes 13%, normal eosinophils3 % and normal monocytes 6 %, high serum phosphorous levels 7.5 mg/dl, high serum urea (urease GLDH) 200.3 mg/dl and high serum creatinine 6.2 mg/dl but low serum calcium levels 5.8 mg/dl, low serum ionized calcium levels 0.60 nmol/l and high alkaline phosphatase levels 1650 u/l, high urine protein(pyrogallo red) 398 mg/dl. and low serum calcidiol 12 nmol/L (normal range 75 to 250 nmol/L). The radiological investigations also confirmed the physical findings that generalized osteopenia, course trabecular changes, widened growth plates, decreased bony length, scoliosis, absence of calcified zone of provisional calcification and bulbous enlargement of the costochondral junctions also known as Rachitic Rosary, skull bossing most commonly in the frontal bone, bilateral tibial and femoral bowing were noted.28

Figure 11: TL-spine lateral view and X-ray pelvis.

X-ray TL-spine lateral view and x-ray pelvis

- L1, L2, L3, L4 vertebra showing concavity of bilateral vertebral end plates.
- Anterior wedging of T12, L1, L2 vertebra noted.
- Increased radiolucency, thinning of the cortex and altered trabecular pattern noted feature suggestive of osteopenia.
- X-ray pelvis: Increased radiolucency of bone noted in bilateral hip bone feature suggestive of osteopenia.
- Trefoil pelvis noted.

X-ray pelvis with bilateral leg

- Increased radiolucency and thinning of the cortex with altered trabecular pattern noted in bones of leg feature suggestive of osteopenia.
- Bowing of long bones of both lower limbs observed with angle formed between the head and neck of femur and its shaft (Mikulicz angle) is less than 120° features suggestive of CoxaVara or Shepherd’s Crook deformity.
- Cortical thickening of bilateral femur was noticed likely to be secondary to repeated fractures.
- Zebra stripe sign noted in long bones of both lower limbs features suggestive of patient have been treated with cyclical bisphosphonate therapy (Pamidronate).

Figure 12: Pelvis with bilateral leg and both hands.

X-ray skull AP and lateral

- Frontal bossing existed
- Abnormal dentiture noted
- Ill-defined radiolucent lesions noted in the skull vault.
- Wormian bone noted in the sagittal and coronal sutures.
- Increased radiolucency of skull bone noted feature suggestive of osteopenia.

X-ray chest

- Costochondral enlargement noted bilaterally at the anterolateral aspect of the rib giving appearance of Rachitic Rosary.
- Violin shape of the chest and abdominal wall also noted.

X-ray bilateral wrist with both hands

- Centers of scaphoid, lunate, trapezium and trapezoid have not appeared.
- Provisional zone of calcification found to be present in metaphyses of distal end of both radius and ulna.
- Praying of metaphyses of distal end of bilateral radius and ulna noted.

In view of osteopenia, abnormal dentiture, Wormian bone, multiple fractures features suggestive of osteogenesis imperfecta tarda type -1. Osteogenesis imperfecta –the term osteogenesis imperfecta encompasses a group of genetic disorders characterised by recurrent multiple fractures, abnormal dentiture,
skeletal fragility, low bone mass and brittle bones variations resulting and ensuing due to mutations in the genes encoding type 1 collagen. The most common features included blue sclera, abnormal dentiture, progressive hearing loss and kyphoscoliosis can impair respiration causing cor pulmonale and predispose to pulmonary infections. On radiographs popcorn like deposits of minerals on the end of long bones further establishes an obvious sign. The biochemical indices of metabolic bone disease were quite normal in osteogenesis imperfecta though resorption markers were often increased when the patient was immobilised. In patients of haploinsufficiency, the bone formation markers plasma procollagen C-terminal peptide and procollagen N— terminal peptide which were derived from type 1 collagen were often relatively low compared to the other formation markers such as bone ALP. In patients with bruck syndrome having osteogenesis imperfecta with contractures, there was defective cross linking of collagen due to mutations in FKBP10 or PLOD2. The usual pyridinoline to deoxypyridinoline ratio in urine gets reversed. There was one another recessive osteogenesis imperfecta variant resulting from mutations in SERPINF1 that encoded pigment epithelium derived factor PEDF, a secreted glycoprotein of as yet uncertain function in bone. PEDF was undetectable in the serum of patients with OI variant.2,8

**Hyypoparathyroidism and pseudohypoparathyroidism**

The term functional hypoparathyroidism refers to a group of metabolic disorders in which hypocalcemia and hyperphosphatemia persist either due to a failure of the parathyroids glands to secrete adequate amounts of biologically active parathyroid hormone (PTH) or, less commonly, due to an inability of PTH to elicit proper biologic responses pertaining to target tissues. Plasma concentrations of PTH show reduced value or absent in patients with true hypoparathyroidism. By contrast, plasma concentrations of PTH found to be typically elevated in patients with pseudohypoparathyroidism (PHP), and reveal utter failure of target tissues to respond properly to the biologic functions of PTH. Thus, true hypoparathyroidism deviates fundamentally and biochemically from PHP.9

**Case report**

A 40 year female patient entered to ortho OPD with chief complaints of pain in right wrist and forearm for the last 15 days with history of self-fall, also complains of aches and tenderness in right forearm associated with severe cramping, intermittent muscular spasms (tetany), carpopedal muscular spasms.

Biochemical findings of the patient were serum calcidiol 56 ng/ml (normal range 30-80 ng/ml), low serum calcium (arsenazo) 6.2 mg/dL, raised serum alkaline phosphatase 569 U/L, high serum phosphorous 6.3 mg/dL, serum sodium 140 meq/L, high serum potassium 6.1 meq/L, TSH 1.9 mIU /mL, Total T3 167 ng /dl, Total T4 7.0 ug /dl, Free T4 1.3 ng /dl, Serum parathyroid hormone level 129pg/mL.

**X ray bilateral wrist with both hands –e/o**

- Cortical thinning and altered trabecular pattern noted. Feature suggestive of osteopenia of visualized bones.
- Non- union fracture noted in distal end of right ulna.(impaired bone healing due to metabolic causes).
- Short metacarpal noted in 4th digit of both hand (a hallmark of pseudohyopoparathyroidism) features suggestive of pseudohyoparathyroidism with gross osteoporotic changes of visualised bones.

![Figure 13: Hypoparathyroidism and pseudohypoparathyroidism.](image)

**Table 1: Blood serum chemistry – Normal values.**

<table>
<thead>
<tr>
<th>Test</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum sodium</td>
<td>135-145 mEq/L</td>
</tr>
<tr>
<td>Serum potassium</td>
<td>3.5 – 5.0 mEq/L</td>
</tr>
<tr>
<td>Serum alkaline Phosphatase</td>
<td>53 – 128 U/L</td>
</tr>
<tr>
<td>Serum phosphorus</td>
<td>Children 4.5-5.5 mg/dL; Adults 2.5 – 4.5 mg/dL</td>
</tr>
<tr>
<td>Serum calcium</td>
<td>8.4-10.4 mg/dL</td>
</tr>
<tr>
<td>Total T4 (ELISA)</td>
<td>5-12 µg/dL</td>
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<tr>
<td>Total T3 (Chemi luminescence)</td>
<td>120-190 ng/dL</td>
</tr>
<tr>
<td>TSH (Radioimmunoassay)</td>
<td>0.5-4.5 mIU/ml</td>
</tr>
<tr>
<td>Free T3 (Chemi luminescence)</td>
<td>0.2-0.5 ng/dL</td>
</tr>
<tr>
<td>Free T4</td>
<td>0.7-1.8 ng/dL</td>
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<tr>
<td>Plasma tyrosine</td>
<td>60-70 µ mol/L</td>
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<tr>
<td>Serum calcidiol</td>
<td>20-40 ng/mL</td>
</tr>
<tr>
<td></td>
<td>75-250 nmol/L</td>
</tr>
</tbody>
</table>

**Discussion and conclusion**

Presence of short stature, obesity, intermittent muscular spasms (tetany), high PTH (due to the low level of calcium in the blood), high serum phosphate, low serum calcium features suggestive of pseudohypo-
parathyroidism). Pseudohypoparathyroidism is a heterogenous group of disorder associated primarily with resistance to the parathyroid hormone and characterized by hypocalcemia, hyperphosphotaemia, increased serum concentration of PTH and insensitivity to the biological activity of PTH. Its pathogenesis has been linked to dysfunctional G proteins.9

CONCLUSION

In cases of rickets and osteomalacia either decreased or normal values of serum calcium and serum phosphorus were obtained. But the cases pertaining to renal failure with rickets values of serum phosphorous were found to be raised. However, in all cases of rickets and osteomalacia values of serum alkaline phosphatase were also found to be raised. Serum alkaline phosphatase is a good marker in rickets and osteomalacia, ICTP in osteoporosis, pyridinoline, deoxypyridinoline in primary hyperparathyroidism, serum PICP in renal osteodystrophy. However, the main use of markers is to establish whether a high bone turnover state exists with its various consequences is a feature of the more common metabolic bone disease and a key target of currently available therapies.

While in cases of primary hyperparathyroidism increased or normal values of serum calcium, parathormone and serum alkaline phosphatase were detected. Cases of patients suffering from secondary hyperparathyroidism increased or normal values of serum phosphorus, parathormone, serum alkaline phosphatase were again observed, but simultaneously decreased or normal values of serum calcium were noticed. In addition to it the patients with tertiary hyper parathyroidism increased or normal values of serum calcium, serum phosphorus and serum alkaline phosphatase were noted irrespective of their age.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES