Causes of Rickets in Renal Diseases

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Abstract

Rickets is a disease common in developing countries many cases are due to poor vitamin D intake or calcium deficiency. However, some cases are refactory to vitamin D Therapy and are related to renal defect as rickets of renal tubular,acidosis, hypophosphatemic rickets and vitamin D dependant rickets. Our study aimed to determine the incidence and characteristics of various causes of bone disease in pediatric renal patients in Abouelrish Children Hospital. The most common causes of renal rickets were found to be hypophosphatemic rickets, followed by renal tubular acidosis and vitamin D resistance the most common manifestations were delayed walking and convulsions (100%) and bow les (75%)

Key words:

(Rickets–Vitamin D deficiency-Renal Tubular Acidosis – Hypophosphatemia)

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List of Abbreviations

ABG	Arterial blood gases
ADHR	Autosomal dominant hypophosphatemic rickets
ALP	Alkaline phosphatase
ARHR	Autosomal recessive hypophosphayemic rickets
Bax	B cell lymphoma associated x protein
BCL2	B cell lymphoma
CKD	Chronic kidney disease
d RTA	Distal renal tubular acidosis
DMP1	Dentin matrix protein -1
DRTA	Distal renal tubular acidosis
FGF- 23	Fibroplast growth factor 23
GFR	Glomerular filtration rate
HHRH	Hereditary hypophosphatemic rickets with hypercalcuria
HVDRR	Hereditary vitamin D resistant rickets
id RTA	Incomplete renal tubular acidosis
IGF-I	Insulin growth factor
LMW	Low molecular weight
mRNA	messenger RNA
NCX1	Na^{+} /Ca^{2+}exchanger
PC-1 gene	plasma cell membrane glycoprotein gene
PEA	Phosphoethanolamine
Phex	phosphate regulating endopeptidase on the X- chromosome
Pi	Inorganic phosphorus
PLP	Pyridoxal 5'phosphate
PMCA1b	Plasma membrane ca ATPase

PO_4	Phosphate
PRTA	Proximal renal tubular acidosis
PTH	Parathyroid hormone
RANKL	Receptor activator of nuclear factor –KB ligand
RTA	Renal tubular acidosis
RXR	Retinoid X receptor
TH	T helper lymphocytes
TIO	Tumour induced osteomalacia
TLRs	Toll like receptors
TmP/GFR	Maximal tubular reabsorption of phosphorus per glomerular filtration rate
TNAP	Tissue non specific alkaline phosphatase
TRP	Total reabsorption of phosphorus
TRPVS	Transient receptor potential cation channel,subfamily V, member 5
VDD	Vitamin D defiency
VDDR	Vitamin D dependant rickets
VDDR-I	Vitamin D dependant rickets type I
VDR	Vitamin D receptor
VDREs	Vitamin D Receptor elements
VDR-RXR	Vitamin D recetor retinoic acid x- receptor complex
VSMCS	Vascular smooth muscles
XLH	X linked hypophosphatemia
XLHR	X linked hypophosphatemic rickets

Introduction

There are several causes for the presence of rickets in association with renal disorders:

The most commonly encountered non-nutritional form of rickets is familial hypophosphatemia. The usual mode of inheritance is X-linked dominant. Autosomal dominant and sporadic forms have also been reported. Pathogenic mechanisms involve defects in the proximal tubular reabsorption of phosphate and in the conversion of 25(OH)D to $1,25(OH)_2$ D. Children with familial hypophosphatemia present with bowing of the lower extremities related to weight bearing at the age of walking. Tetany is not present, and the profound myopathy, rachitic rosary, and Harrison groove (pectus deformity) characteristic of calcium-deficient rickets are not evident. The adult height of untreated patients is 130–165 cm. Pulp deformities and lesions of intraglobular dentin are characteristic tooth abnormalities ***(Alon, 2006).***

Rickets may be present in primary renal tubular acidosis (RTA), particularly in type II or proximal RTA. Hypophosphatemia and phosphaturia are common in these syndromes, which are characterized by hyperchloremic metabolic acidosis, various degrees of bicarbonaturia, and, frequently, hypercalciuria and hyperkaluria. Bone demineralization without overt rickets usually is detected in type I and distal RTA ***(Sharma et al., 2007).***

Patients with nephropathic cystinosis present with clinical manifestations reflecting their pronounced tubular dysfunction and Fanconi syndrome, including polyuria and polydipsia, growth failure, and rickets. Fever, caused by dehydration or diminished sweat production, is common. Patients are typically fair skinned and blond, owing to diminished pigmentation. Photophobia occurs. Retinopathy and impaired

visual acuity occur, with progressive tubulointerstitial fibrosis, renal insufficiency is invariant,hypothyroidism, hepatosplenomegaly, and delayed sexual maturation ***(Bökenkamp and Ludwig, 2011).***

Lowe syndrome (also called oculocerebrorenal syndrome of Lowe) is a rare X-linked disorder characterized by congenital cataracts, mental retardation, and Fanconi syndrome ***(Bockenhauer et al. 2008).***

Finally, renal osteodystrophy with its characteristic impaired renal production of 1,25-dihydroxycholecalciferol, hyperphosphatemia, hypocalcemia, and secondary hyperparathyroidism may be seen in cases of chronic kidney disease. Muscle weakness, bone pain, and fractures with minor trauma are all presenting features of this syndrome ***(Sprague, 2010).***

Aim of work

To determine the incidence of rickets secondary to renal disease and its etiologic types and presenting manifestations and laboratory characteristics in renal patients attending the outpatient pediatric renal clinic in Abou Elrish Hospital.

Normal bone

Bone is the basic unit of the human skeletal system and provides the framework for and bears the weight of the body, protects the vital organs, supports mechanical movement, hosts hematopoietic cells, and maintains iron homeostasis ***(Dengzl et al ., 2008).***

Bone Formation:

The formation of bone during the fetal stage of development occurs by two processes: Intramembranous ossification and endochondral ossification.

A. Intramembranous ossification:

Intramembranous ossification mainly occurs during formation of the flat bones of the skull but also the mandible, maxilla, and clavicles; the bone is formed from connective tissue such as mesenchyme tissue rather than from cartilage. The steps in intramembranous ossification are:

1. Development of ossification center
2. Calcification
3. Formation of trabeculae
4. Development of periosteum

B. Endochondral ossification:

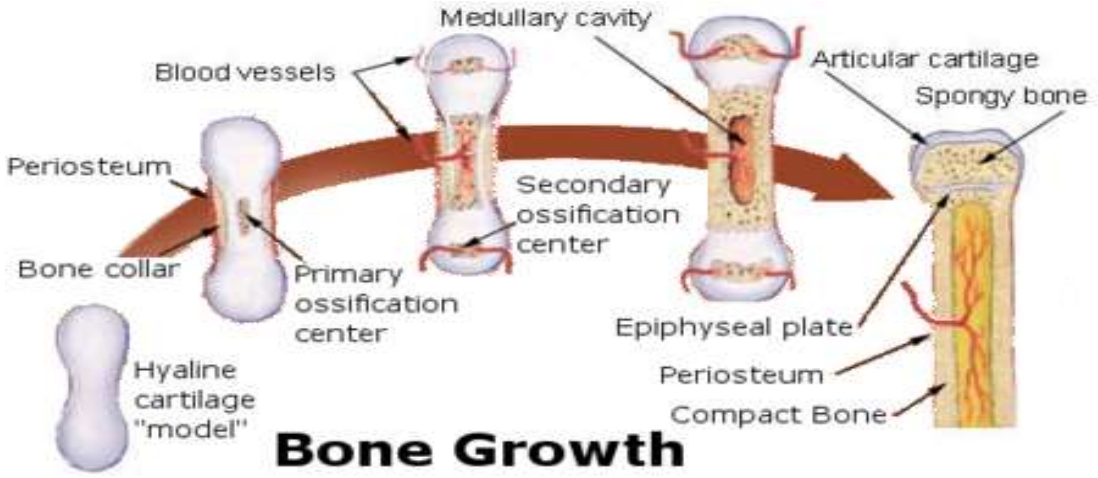

Figure (1): Bone Growth

Endochondral **ossification**, on the other hand, occurs in long bones and most of the rest of the bones in the body; it involves an initial hyaline cartilage that continues to grow. The steps in endochondral ossification are:

1. Development of cartilage model
2. Growth of cartilage model
3. Development of the primary ossification center
4. Development of the secondary ossification center
5. Formation of articular cartilage and epiphyseal plate

Endochondral ossification begins with points in the cartilage called "primary ossification centers." They mostly appear during fetal development, though a few short bones begin their primary ossification after birth. They are responsible for the formation of the diaphyses of long bones, short bones and certain parts of irregular bones. Secondary ossification occurs after birth, and forms the epiphyses of long bones and the extremities