Introduction

Rickets was unknown to a rare occurrence for the ancient civilization of Egypt. The signs of rickets are absent from the ancient writings, because early civilization was in warm climates with clear skies (sun shine) and with population spending much time outdoors ***(McDowell, 2013).***

Later, rickets start to appear as a result of pollution that hinders cutaneaus synthesis of vitamin D as well as nutritional insufficient intake of vitamin D resources ***(Perlstein, 2012)***.

Rickets is most common in children ages 6 to 24 months. Children are at the highest risk of rickets because they are still growing ***(Cafasso, 2012)***. Children might not get enough vitamin D if they live in a climate with little sunlight, have dark skin, do not drink milk products, or follow a vegetarian diet. In some cases, the condition is hereditary ***(Cafasso, 2012).***

Lipid peroxidation is a process generated naturally in small amounts in the body, mainly by the effect of several reactive oxygen species (hydroxyl radical, hydrogen peroxide etc.). These reactive oxygen species readily attack the polyunsaturated fatty acids of the fatty acid membrane leading to its destruction. The end-products of such lipid peroxidation reactions (including MDA) are dangerous for the viability of cells and tissues ***(Mylonas and Kouretas, 1999)***.

Enzymatic (e.g., catalase, superoxide dismutase) and non enzymatic (e.g., vitamins A and E) are natural antioxidant defense mechanisms; however, these mechanisms may be overcome, causing lipid peroxidation to take place ***(Mylonas and Kouretas, 1999)***.

Increased incidence of infection has long been recognized as a part of nutritional rickets. These repeated infections could be attributed to disturbed lymphocyte survival as well as vitamin D deficiency ***(El Hodhod et al., 2006)***. Disturbed oxidant antioxidant status may also have a contributing role but it is not fully investigated.

Aim of the Work

The aim of this work was to study Oxidant antioxidant status in infants with nutritional rickets in order to know if it has a role in repeated infections in these cases.

Rickets

Definition:

Rickets is a disease of growing bone that is due to immineralized matrix at the growth plates and occurs only in children before fusion of the epiphysis. Rickets is a disorder caused by lack of vitamin D, calcium, or phosphate. It leads to softening and weakening of the bones ***(Greenbaum, 2011).***

Etiological classification:

There are several subtypes of rickets, including hypophosphatemic rickets (vitamin-D-resistant rickets), renal or kidney rickets (renal osteodystrophy), and most commonly, nutritional rickets ***(Perlstein, 2012).*** Causes of rickets are demonstrated in table (1).

Vitamin D deficiency rickets (Infantile Rickets)

Vitamin D deficiency remains the most common cause of rickets globally and is prevalent, even in industrialized countries. Vitamin D can be obtained from dietary sources or from cutaneous synthesis in response to exposure to ultraviolet B rays of the sun ***(Greenbaum, 2011).***

Table (1): Etiological classification of rickets

Vitamin D Disorders	**Phosphorus Deficiency**
Nutritional vitamin D deficiency Congenital vitamin D deficiency Secondary vitamin D deficiency Malabsorption Increased degradation Decreased liver 25-hydroxylase Vitamin D–dependent rickets type 1 Vitamin D–dependent rickets type 2 Chronic renal failure	Inadequate intake Premature infants (rickets of prematurity) Aluminum-containing antacids
Calcium Deficiency	**Renal Losses**
Low intake Diet Premature infants (rickets of prematurity) Malabsorption Primary disease Dietary inhibitors of calcium absorption	X-linked hypophosphatemic rickets* Autosomal dominant hypophosphatemic rickets* Autosomal recessive hypophosphatemic rickets* Hereditary hypophosphatemic rickets with hypercalciuria Overproduction of phosphatonin Tumor-induced rickets* McCune-Albright syndrome* Epidermal nevus syndrome* Neurofibromatosis* Fanconi syndrome Dent disease Distal renal tubular acidosis

*Disorders secondary to excess phosphatonin

(Greenbaum, 2011)

Physiology of vitamin D

Vitamin D is synthesized in skin epithelial cells by conversion of 7-dehydrochlesterol to vitamin D3 (3-cholecalciferol) by ultraviolet B radiation from the sun. After absorption, Vitamin D is then transported bound to vitamin D-binding protein to the liver, where 25-hydroxlase converts vitamin D into 25-hydroxy vitamin D (25-D), the most abundant circulating form of vitamin D ***(Greenbaum, 2011).***

The final step in activation occurs in the kidney, where 1α-hydroxylase adds a second hydroxyl group, resulting in 1,25-dihydroxy vitamin D (1,25-D) ***(Greenbaum, 2011).***

The 1α-hydroxylase is up regulated by PTH and hypophosphatemia; hyperphosphatemia and 1,25-D inhibit this enzyme. 1,25-D acts by binding to an intracellular receptor and in the intestine, this binding results in marked increase in calcium absorption, which is highly dependent on 1,25-D. There is also an increase in phosphorus absorption, but this effect is less significant because most dietary phosphorus absorption is vitamin D independent. 1,25-D also has direct effects on bone, including mediating resorption. 1,25-D directly suppresses PTH secretion by the parathyroid gland, thus completing a negative feedback loop. PTH secretion is also suppressed by the increase in serum calcium mediated by 1,25-D. 1,25-D inhibits its own synthesis in the kidney and increases the synthesis of inactive metabolites ***(Greenbaum, 2011).***

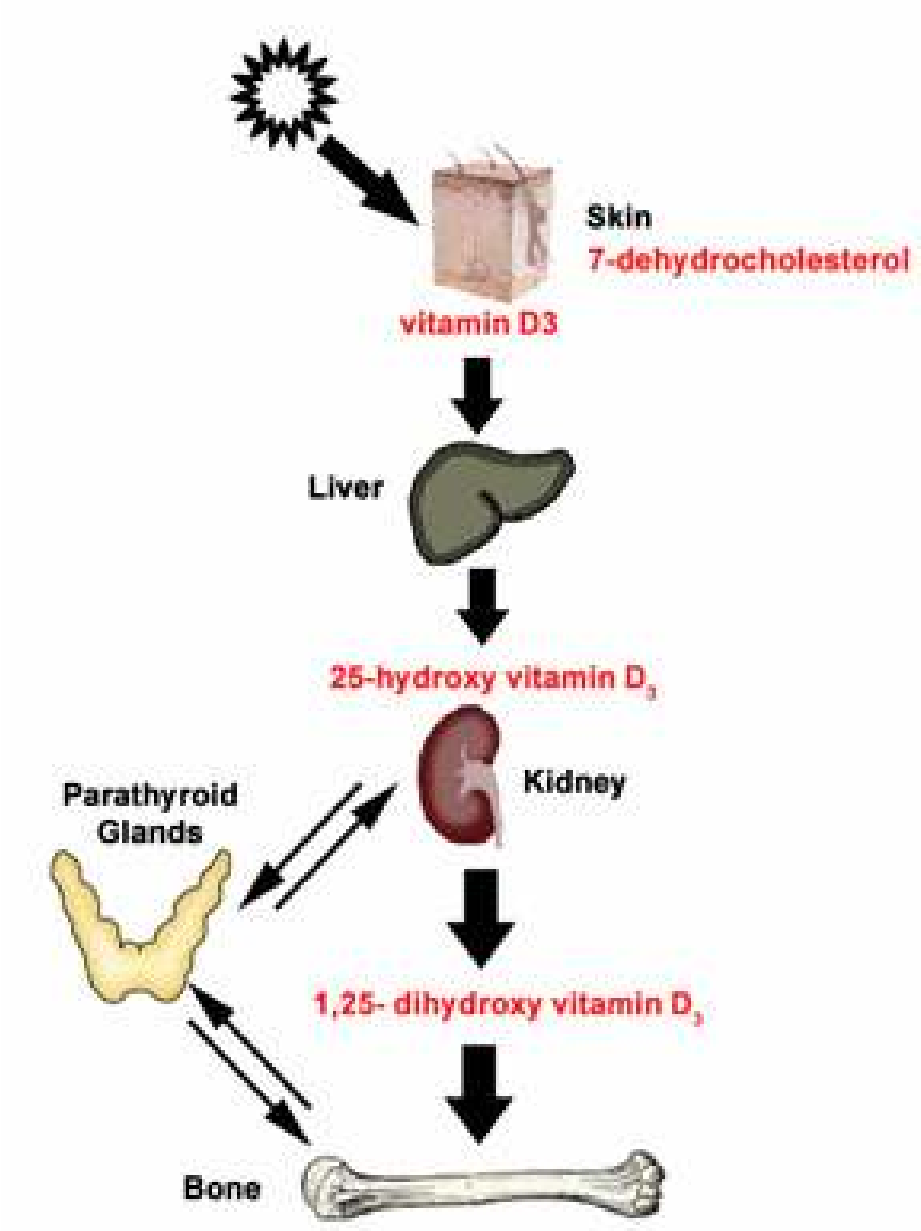

Fig. (1): Physiology of vitamin D ***(Narchi, 2001)***

Sources of vitamin D:

Physical and metabolic characteristics and food sources of vitamin D are demonstrated in table (2).

Table (2): Sources and characteristics of vitamin D

Names and synonyms	Characteristics	Biochemical action	Effects of deficiency	Effects of excess	Sources
Vitamin D3 (3-cholecalciferol), which is synthesized in the skin, and vitamin D2 (from plants or yeast) are biologically equivalent; 1 μg = 40 IU vitamin D	Fat-soluble, stable to heat, acid alkali, and oxidation; bile necessary for absorption; hydroxylation in the liver and kidney necessary for biologic activity	Necessary for GI absorption of calcium; also increases absorption of phosphate; direct actions on bone, including mediating resorption	Rickets in growing children; osteomalacia; hypocalcemia can cause tetany and seizures	Hypercalcemia, which can cause emesis, anorexia, pancreatitis, hypertension, arrhythmias, CNS effects, polyuria, nephrolithiasis, renal failure	Exposure to sunlight (UV light); fish oils, fatty fish, egg yolks, and vitamin D–fortified formula, milk, cereals, bread

(Greenbaum, 2011)

Epidemiology:

Children with the following conditions are at higher risk for developing vitamin D deficiency rickets: limited sun exposure, lack of vitamin D in diet, gastrointestinal diseases associated with vitamin D malabsorption as cystic fibrosis and celiac disease and presence of liver or kidney disease. Children with dark skin may have a decreased ability to synthesize vitamin D in response to sunlight as melanin has been shown to inhibit the production of vitamin D by the skin ***(Burgener et al, 2008).***

The peak prevalence of vitamin D deficient rickets is characteristically between 6 and 18 months of age, with a further smaller peak occurring during adolescence ***(Pettifor, 2008).***

Globally, nutritional deficiencies are the leading cause of rickets, followed by vitamin D-dependent, vitamin D-resistant, and renal rickets. Surprisingly, in the sunniest areas of the world, rickets is still a major health problem. Reasons for this include over-wearing practices, avoidance of exposure of any skin to sunlight, and foods unfortified with vitamin D. Darker-pigmented people also require more sun exposure than lighter-skinned people, to form bioactive vitamin D. Increased sunscreen use has also been implicated ***(Diehl and Chiu., 2010).***

Incidence and prevalence:

Rickets is still prevalent in Egypt in spite of the advances in the socioeconomic status. The incidence of rickets among Egyptians during the first two years of life was reported to be 12-31.1% ***(El-Bishlawy et al., 1992).***

In developed countries, rickets is a rare disease; incidence is less than 1 in 200,000. The CDC estimates 5 per 1,000,000 children aged between 6 months and 5 years have rickets ***(Nilde et al., 2006).***

Clinical Manifestations

The chief complaint in a child with rickets is quite variable. Many children present because of skeletal deformities, where as others have difficulty walking owing to a combination of deformity and weakness. Other common presenting complaints include failure to thrive and symptomatic hypocalcaemia ***(Greenbaum, 2011).*** Table (3) and figure (2) demonstrates the common clinical features of rickets.

Table (3): Common clinical features of rickets

General
Failure to thrive Restlessness Protruding abdomen Muscle weakness (especially proximal) Fractures
Head
Craniotabes Frontal bossing Delayed fontanel closure Delayed dentition; caries Craniosynostosis
Chest
Rachitic rosary Harrison groove Respiratory infections and atelectasis*
Back
Scoliosis Kyphosis Lordosis
Extremities
Enlargement of wrists and ankles Valgus or varus deformities Windswept deformity (combination of valgus deformity of 1 leg with varus deformity of the other leg) Anterior bowing of the tibia and femur Coxa vara Leg pain
Hypocalcemic Symptoms†
Tetany Seizures Stridor due to laryngeal spasm

*These features are most commonly associated with the vitamin D deficiency disorders.
†These symptoms develop only in children with disorders that produce hypocalcemia

(Greenbaum, 2011)

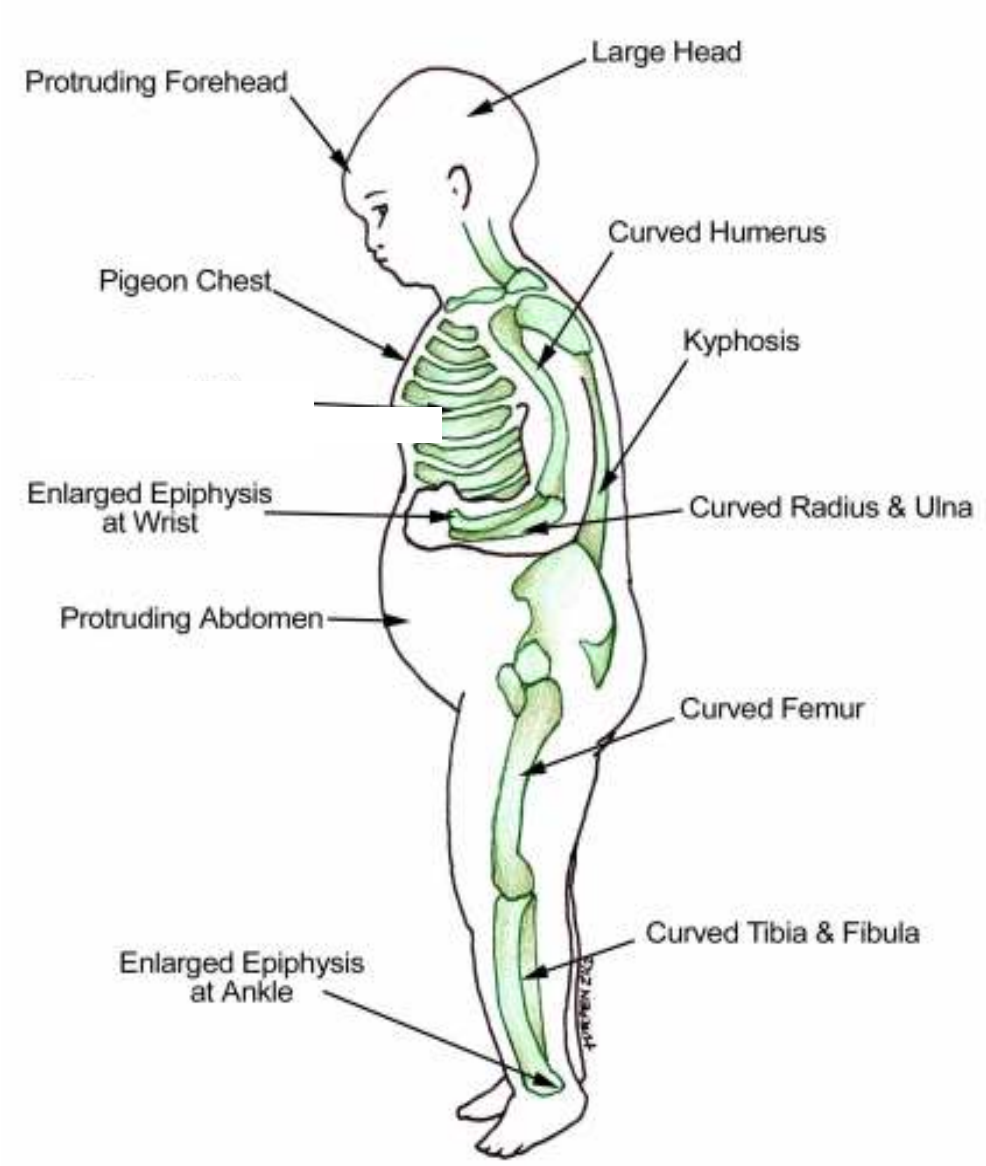

Fig. (2): Findings in patients with rickets ***(Rijn and McHugh, 2011)***

Craniotabes

Craniotabes is a softening of the cranial bones and can be detected by applying pressure at the occiput or over the parietal bones. The sensation is similar to the feel of pressing into a Ping-Pong ball and then releasing. Craniotabes may also be secondary to osteogenesis imperfecta, hydrocephalus, and syphilis. It is a normal finding in many newborns, especially near the suture lines, but it typically disappears within a few months of birth ***(Greenbaum, 2011).***

Rachitic rosary:

Widening of the costochondral junctions results in a rachitic rosary, which feels like the beads of a rosary as the examiner's fingers move along the costochondral junctions from rib to rib (Figure 3) ***(Greenbaum, 2011).***

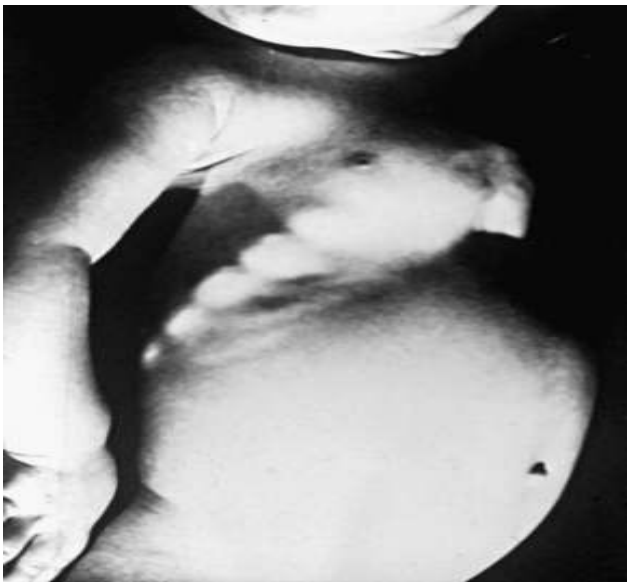

Fig. (3): Rachitic Rosary ***(Greenbaum, 2011)***

Enlargement at the wrists and ankles:

Growth plate widening is also responsible for the enlargement at the wrists and ankles ***(Greenbaum, 2011).***

Harrison groove

The horizontal depression along the lower anterior chest occurs from pulling of the softened ribs by the diaphragm during inspiration (Figure 4) ***(Greenbaum, 2011).***

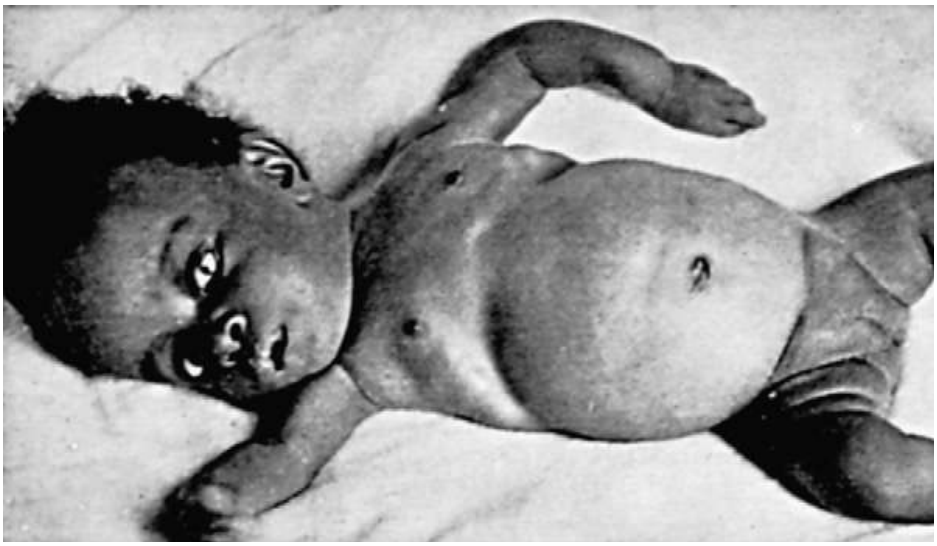

Fig. (4): Harrison groove ***(Greenbaum, 2011)***

Complication:

If left untreated, a child with rickets is more prone to fractures of the bone, bone deformities, severely low blood calcium levels that can lead to cramps, seizures and breathing problems. Softening of the ribs also impairs air movement and predisposes patients to atelectasis and pneumonia. Heart muscle weakness – can occur but it is rare ***(Brunner and Stephanie, 2013).***

Diagnosis

Diagnosis of vitamin D deficiency rickets depend on typical nutritional history of poor vitamin D intake, characteristic clinical manifestation and is confirmed by radiological and laboratory manifestation ***(Perlstein, 2012).***

Radiological manifestation:

Signs of active rickets:

Rachitic changes are most easily visualized on posteroanterior radiographs of the wrist, although characteristic rachitic changes can be seen at other growth plates.

1-Fraying:

Decreased calcification leads to thickening of the growth plate. The edge of the metaphysis loses its sharp border ***(Greenbaum, 2011).***

2- Cupping:

The edge of the metaphysis changes from a convex or flat surface to a more concave surface. This is most easily seen at the distal ends of the radius, ulna, and fibula ***(Greenbaum, 2011).***

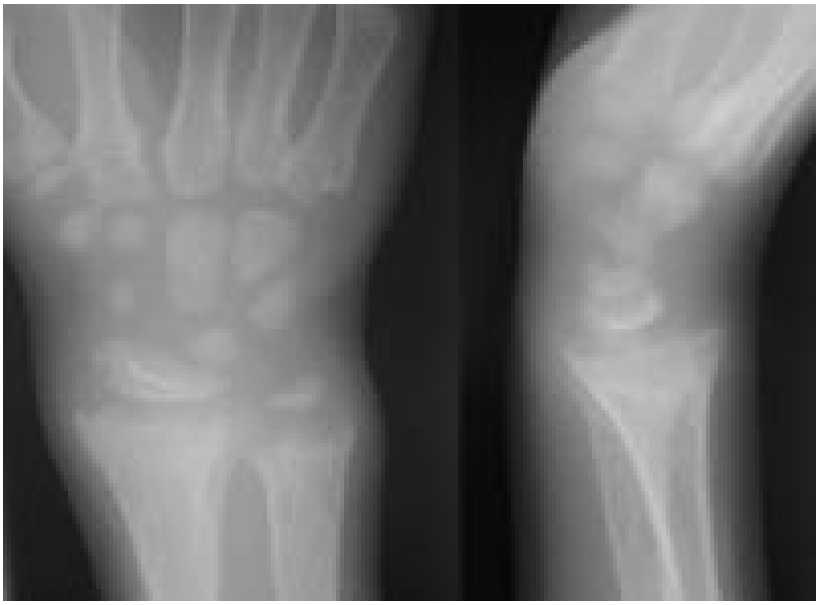

Fig. (5): Radiological findings of active rickets: Anteroposterior and lateral radiographs of the wrist of an 8-years-old boy with rickets demonstrating cupping and fraying of the metaphyseal region *(Rijn and McHugh, 2011).*

3- Broadening:

There is widening of the distal end of the metaphysis, corresponding to the clinical observation of thickened wrists and ankles as well as the rachitic rosary ***(Greenbaum, 2011).***

4- Deformity of long bones such as bowing of legs (genu varum) or knock knees (genu valgum) ***(Rijn and McHugh, 2011).***