CALCIUM HOMEOSTASIS IN ACTIVE AND HEALED RICKETS

THESIS

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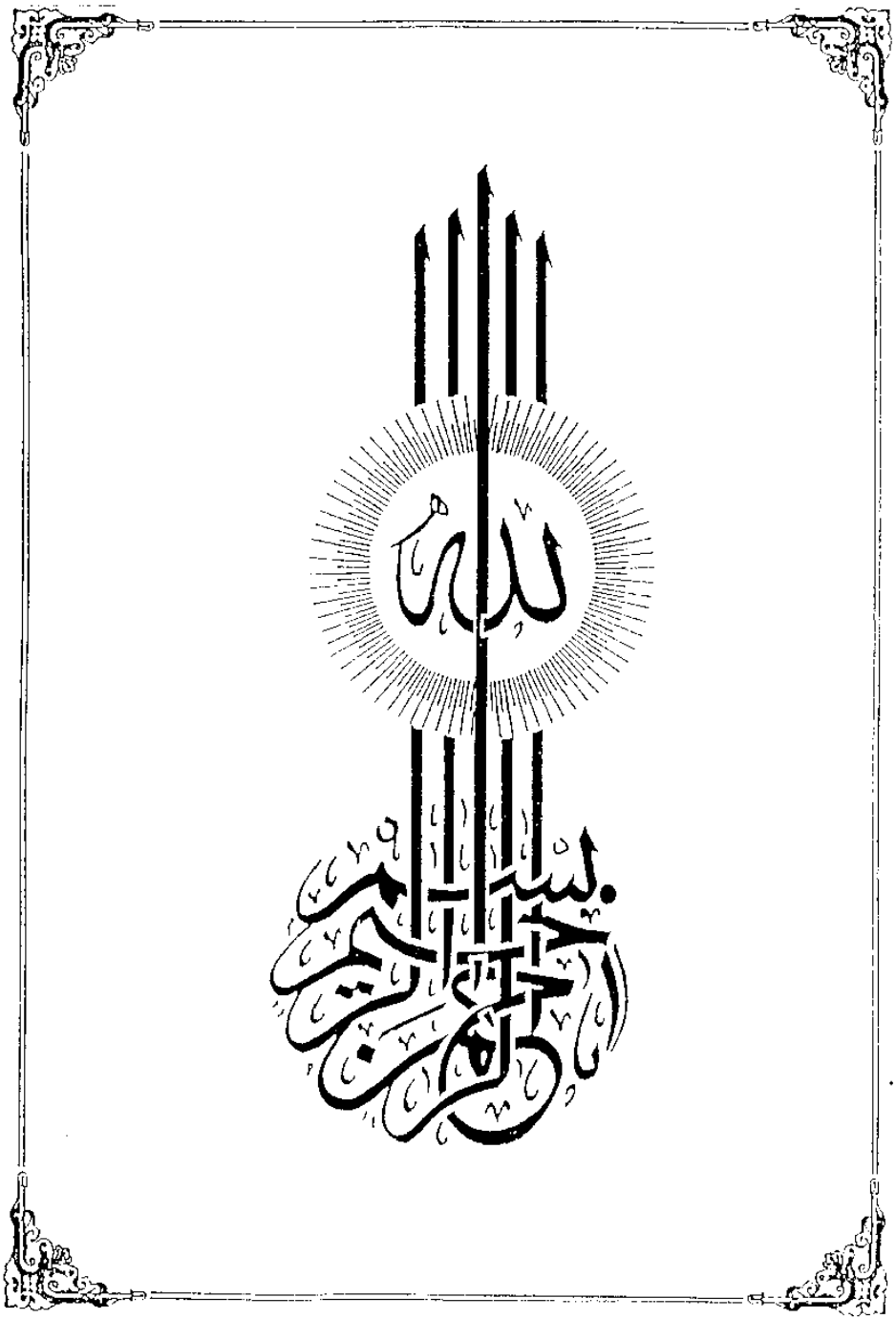

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Introduction & Aim Of The Work

INTRODUCTION and AIM OF THE WORK

Rickets is a term applied to an abnormality of growing bones related to lack of vitamin D, lack of alkaline phosphatase or imbalance of plasma calcium and phosphorus. This disease has occurred throughout the world and there are a range of causes for such abnormality .

Parathyroid hormone, calcitonin and vitamin D play primary role in regulating the movement of calcium and phosphorus into and out of cells and in controlling the mineralization of bones and teeth **(Forfar and Arneil, 1984)** .

Parathyroid hormone increases plasma calcium primary by mobilizing this ion from bone and its reabsorption in the renal tubules. 1.25 dihydroxycholecalciferol increases plasma calcium by increasing intestinal absorption of calcium, and mobilizing calcium from bone. Calcitonin decreases plasma calcium by inhibiting bone resorption. It also decreases renal formation of 1.25 dihydroxycholecalciferol **(Ganong, 1977)**, but the exact physiologic role of calcitonin is uncertain **(Nelson et al, 1983)** .

The aim of this work is to study the role of parathyroid hormone and calcitonin in regulating calcium and phosphorus homeostasis in active and healed rickets hoping to early diagnosis, prevention and treatment of this major illness among our children .

Review Of Literature

REVIEW OF LITERATURE

RICKETS

DEFINITION :

Rickets is defined as the failure of bone matrix to mineralize at an appropriate rate, owing to inadequate concentrations of calcium ion and monohydrogen phosphate in body fluids; this results in accumulation of mineralized osteoid **(Stanbury, 1972)** .

Rickets occurs in growing children whereas in adults in whom linear growth has been completed, lack of vitamin D leads to osteomalacia. In children manifestations of rickets depend on the age of onset and chronicity of metabolic disorder. Serum concentrations of calcium and phosphate are usually low normal or low, whereas skeletal alkaline phosphatase activity is high **(Root and Harrison, 1976)** .

INCIDENCE :

The incidence of rickets among Egyptians during the first two years of life was reported to be **12 - 13 %** **(Khalifa et al, 1971 ; Awwaad et al, 1975)** .

It is still a commonly recognized disease in Egypt inspite of adequate sunlight and real advances in socio-economic status .

The factors responsible for the occurrence of rickets in **Egypt** are repeated pregnancies without proper spacing young aged non educated mothers, the habit of excessive rapping of children and keeping them indoors without exposure to sun, poor housing, inadequate feeding and prevalence of gastroenteritis **(Massoud et al, 1982)** .

CLASSIFICATION :

The various forms of rickets can be classified into:

(A) Deficiency of active vitamin D metabolite with secondary hyperparathyroidism

1- Vitamin D deficiency
   - a. Congenital
   - b. Prematurity
   - c. Infantile
   - d. Toddler
   - e. Adolescent Asian
   - f. Sub-clinical

2- Malabsorptive states
   - a. Coeliac syndrome, sprue
   - b. Hepatic dysfunction
   - c. Biliary atresia
   - d. Phosphate deficiency or malabsorption
     - * Parenteral hyperalimentation
     - * Low phosphate intake

3- Anticonvulsant drugs

4- Chronic renal disease

5- Vitamin D dependency, 1∝- hydroxylase abnormality.

(B) **Target cell abnormality with renal hypophosphatemia (no secondary hyperparathyroidism)**

1- Fanconi syndrome

a. Cystinosis

b. Tyrosinosis

c. Wilson disease

d. Galactosemia

e. Familial fructose intolerance

f. Lowe syndrome

2- Renal tubular acidosis

3- Familial hypophosphatemia

4- Hypophosphatemia with " non endocrine tumors " (Oncogenic hypophosphatemia)

(C) **End organ resistance to 1.25 $(OH)_2$ D_3**

(D) **Related conditions resembling rickets**

1- Hypophosphatesia

2- Metaphyseal dysostosis

(Root and Harrison, 1976)

Nutritional rickets (vitamin D deficiency)

I. Aetiology :

By definition the cause of the disease is an insufficient intake of vitamin D to promote normal bone growth and to prevent the occurrence of specific abnormal changes in bone. Vitamin D deficiency is due to either dietary lack or absence of sunshine **(Deluca, 1976)** .

After absorption, vitamin D passes through the alimentary lymphatics and is stored in the liver until metabolized. Appropriate plasma concentrations of calcium and phosphate are required for proper ossification together with an appropriate concentration of alkaline phosphatase. Active rickets is most likely to occur during the times of greatest growth as in the preterm infant, and the first year of life **(Fraser et al, 1980)** .

II. Pathogenesis:

The initial pattern seems to be loss of normal calcification of the metaphyses of long bones together with loss of radiological definition of the metaphyseal ends e.g. of radius and ulna. This stage of minimal active rickets **(MAR)** which is subclinical (i.e. not detected clinically) may or may not be accompanied by a high level of alkaline phosphatase and the serum 25-hydroxycholecalciferol **(25 - HCC)** level is usually low **(Richards et al, 1968)**. When supplies of vitamin D increase a denser