

**PYRIDOXINE STATUS IN
VITAMIN D-DEFICIENCY RICKETS**

THESIS

**Submitted for partial fulfillment of
Master degree in Pediatrics**

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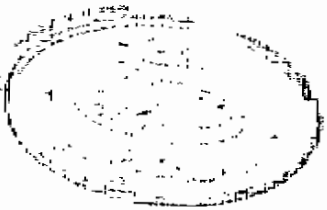
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« وَفِي الْأَرْضِ آيَاتٌ لِلْمُوقِنِينَ
 وَفِي أَنْفُسِكُمْ أَفَلَا تُبْصِرُونَ »
 (النَّازِعَات ٢٠-٢١)
 صَدَقَ اللَّهُ الْعَظِيمُ

On the Earth are signs for those of assured
 faith, as also in your own selves will you not
 then see ?

Holy Koran (S 51 V 20 — 21)



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*Dr. Mohamed Taha,
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**** List of abbreviations ****

<i>ADH.</i>	Anti diuretic hormone.
<i>ALB.</i>	Albumin.
<i>ALP.</i>	Alkaline phosphatase.
<i>Ca.</i>	Calcium.
<i>CFU.</i>	Colony forming unit.
<i>EDTA.</i>	Ethylene diamine tetra-acetic acid.
<i>FSH.</i>	Follicle stimulating hormone.
<i>Hb.</i>	Hemoglobin.
<i>KAU</i>	King Armstrong unit.
<i>MCH.</i>	Mean corpuscular hemoglobin.
<i>MCHC.</i>	Mean corpuscular hemoglobin concentration.
<i>MCV.</i>	Mean corpuscular volume.
<i>PL.</i>	Pyridoxal.
<i>PLP.</i>	Pyridoxal 5-phosphate.
<i>PM.</i>	Pyridoxamine.
<i>PMP.</i>	Pyridoxamine phosphate.
<i>PX.</i>	Pyridoxine.
<i>R.B.Cs.</i>	Red blood cells.

**INTRODUCTION &
AIM OF THE WORK**

B₆ DEFICIENCY AS A CONTRIBUTING FACTOR IN CAUSATION OF ANEMIA WITH RICKETS

INTRODUCTION AND AIM OF THE WORK :-

Alkaline phosphatase (ALP) is a unique plasma membrane bound enzyme whose physiologic role remains poorly defined despite intensive investigations [Mc Comb et al., 1979].

Biochemical studies, including amino acid sequence analysis of both partial proteolytic peptide digests and NH₂ Terminal regions of ALP purified from normal human tissues suggested that there is isoenzymes, each coded by separate genes, occur in man [Sussman et al., 1984]. They have been generally referred to as placental, intestinal, and tissue non specific (bone / liver / kidney) ALP. Posttranslational modifications account for the well-documented physiochemical difference in the tissue non specific ALP family: bone, liver, and kidney are therefore secondary isoenzymes [Mc Comb et al., 1979].

Vitamin B₆ is the generic term for the closely related and interconvertible compounds, i.e. pyridoxine (PN, the alcohol), pyridoxal (PL, the aldehyde), and pyridoxamine

(PM, the amine). Three dietary sources of B₆ are each normally converted in the liver to pyridoxal 5-phosphate (PLP). Organ ablation studies in dogs indicate that mammalian liver is the principle source of circulating PLP, where ~95% is protein bound. Before it can act peripherally, circulating PLP is dephosphorylated to PL, B₆ vitamin that can traverse plasma membranes. Within the cells, PL is converted to B₆ cofactor forms PLP and pyridoxime 5-phosphate (PMP) [Shideler et al., 1983].

Intracellular levels of PLP are regulated by multiple factors including protein binding of PLP, product inhibition of PLP / PMP oxidase by PLP, and phosphatase activity. Ultimately, intracellular B₆ is degraded primarily to 4-pyridoxic acid (4-PA), which is excreted in urine [Shidler et al., 1983].

There are a variety of evidences that ALP acts in the metabolism of vitamin B₆. In vitro PLP has been shown to be hydrolyzed by leukocyte subcellular organelles which are rich in ALP activity, and an inverse relationship has been reported between the PLP concentration and ALP activity in leukocytes. Furthermore, ALP purified from rat liver plasma membranes has been shown to hydrolyze PLP [Lumeng et al., 1975].

In vitro circulating PLP concentration has been associated with increased circulating ALP activity [Labadarios et al, 1977]. Indeed, Anderson and colleagues in 1980 have demonstrated an inverse relationship between circulating PLP levels and ALP activity in patients with either hepatobiliary or bone diseases.

Whyte in 1985 reported that there was markedly increased circulating concentrations of PLP level in hypophosphatasia and his finding identify increased circulating PLP concentration as a marker for hypophosphatasia and provide further evidence that tissue non specific ALP acts in vitamin B₆ metabolism.

It has been shown that in rats the level of vitamin B₆ (PLP) decreased during pregnancy and that this depression was not overcome by large amounts of dietary vitamin B₆ [Sloger et al, 1980]. One aspect that has not been considered in the assessment of vitamin B₆ nutritional status in pregnancy is the possible effect of alkaline phosphatase (ALP), produced by the placenta on circulating PLP and PL levels [Hendrick et al, 1987].

In active rickets serum ALP is usually increased to 20 - 30 units /dl in mild rickets and 60 units or more /dl in severe rickets [Krme et al., 1983].

Also anemia is one of the manifestations that may appear in vitamin B₆ deficiency [Harper et al., 1977].

So we can expect that vitamin B₆ status may be lowered in rickets due to high ALP enzyme and that may be responsible as one of the causes of anemia with rickets.

REVIEW OF LITERATURE

VITAMIN D

In recent years there have been a number of major advances in our understanding of vitamin D metabolism. These new informations on the physiology of vitamin D has greatly improved our understanding of a number of disorders. Vitamin D is actually a group of compounds whose basic structure is related to that of cholesterol [Wellington, 1983].

Types of vitamin D :-

We have at least 10 types of vitamin D which differ from each other in their chemical structure as well as in their antirachitic potency. Only 2 types of vitamin D are naturally occurring and are of biological importance :

Vitamin D₂ (calciferol) :-

It is of plant origin. its precursor is ergosterol. It is manufactured by the action of ultraviolet on a sterol found in fungi and yeasts. It occurs rarely in nature.

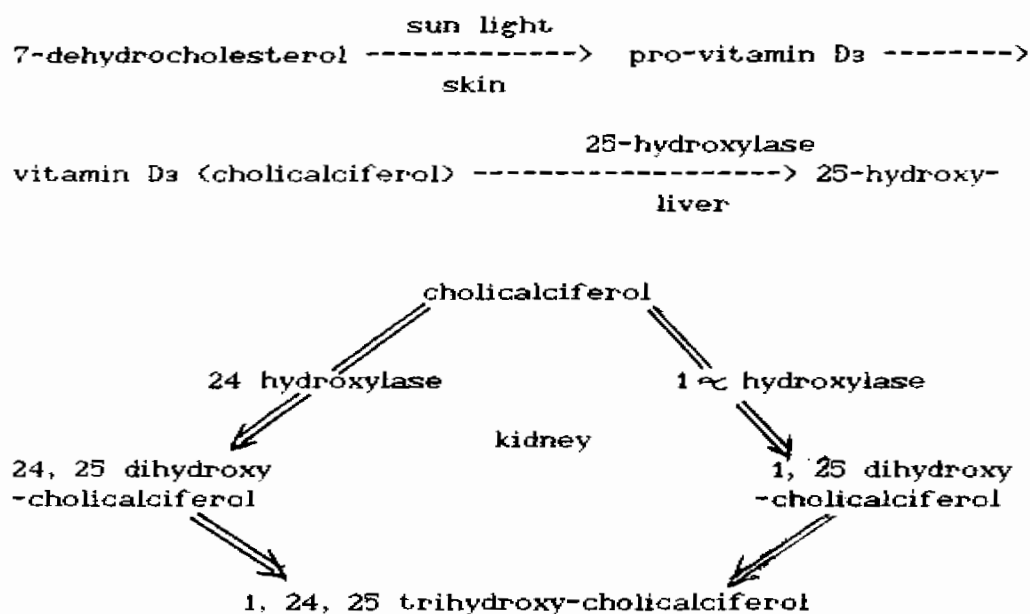
Vitamin D₃ (cholicalciferol) :-

It is of animal origin, its precursor is 7-dehydro-cholesterol present in superficial layers of the skin where it can be activated by ultraviolet sun rays. It is the

natural form of the vitamin which occurs in man and other animals. Adequate exposure to ultraviolet light is necessary, with more exposure being required for darker skinned races [West, 1984].

Absorption of vitamin D :-

Both vitamin D₂ and vitamin D₃ are absorbed from the small intestine, vitamin D₃ may be absorbed more completely and more rapidly. The exact portion of the gut that is most effective in vitamin D absorption may be function of the vehicle in which the vitamin is suspended or dissolved. Bile is essential for adequate intestinal absorption and deoxycholic acid is the most important constituent of bile in this regard. Thus hepatic or biliary dysfunction may impair absorption of vitamin D, other abnormalities of gastrointestinal function especially those associated with steatorrhea, may interfere with absorption of orally administered vitamin D [Gilman et al., 1980].

Metabolism of vitamin D :-

After absorption, the vitamin is distributed in fat and muscles. It undergoes a series of further metabolic conversions.

In the liver, vitamin D₃ is converted to 25-hydroxy-cholicalciferol, which in turn is converted to the active metabolite, 1, 25 dihydroxy cholicalciferol in the kidney.

The normal plasma level of 25-hydroxy-cholicalciferol is about 30 ng/ml., and that of 1, 25 dihydroxy-cholicalciferol is about 0.03 ng/ml. The less