# THIAMINE STUDY IN PROTEIN ENERGY MALNUTRITION

**THESIS**

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Presented

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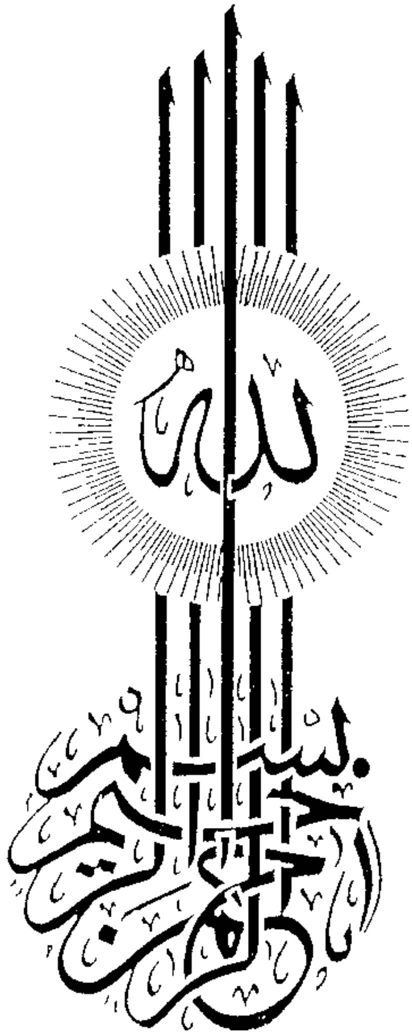
بسم الله الرحمن الرحيم

" سبحانك لا علم لنا إلا ما علمتنا إنك أنت العليم الحكيم"

صدق الله العظيم

سورة البقرة آيه ٣٢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# *List of Abbreviations*

A. M. P : Adenine monophosphate .

A. T. P : Adenine triphosphate .

Cm : Centimeter .

dl : Deciliter .

E. P. O : Erythropoietin .

F. A. D : Flavin adenine dinucleotide .

Fig : Figure .

Gm : Gram

$K^+$ : Potassium

Kg : Kilogram

Kwo : Kwashiorkor

mg : Milligram

ml : Millimeter

mm : Millimeter .

$Na^+$ : Sodium .

P. C. M. : Protein Calorie malnutrition .

P. E. M : Protein energy malnutrition .

R : Correlation Coefficient .

T. P. P : Thiamine Pyrophosphate .

µg : Microgram .

Wt : Weight .

# *INTRODUCTION AND AIM OF THE WORK*

# Introduction

Malnutrition is one of the leading causes of mortality and morbidity in childhood . Malnutrition is due to deficiency of one or more of food stuffs with normal total caloric supply in protein energy malnutrition, although deficiency of calories and other nutrients complicate the clinical and chemical patterns, the principle symptoms are due to insufficient intake of protein of high biological value . ( Barness, 1992 )

Protein energy malnutrition may be not only due to insufficient intake of proteins but also could be due to impairement of absorption of protein, abnormal losses of protein and failure of protein synthesis . ( Barness, 1992 )

Edema usually develops early in protein energy malnutrition, failure to gain weight is masked by edema which is often present in internal organs before it can be recognized in the face and limbs . Some researchs have suggested that hypoalbuminemia is a major cause of edema in kwashiorkor ( Coward et al., 1979 ), while others beleive that hypoalbuminemia plays an insignificant role

( Golden et al., 1980 )

Laditan (1984) proved that there is a significant negative correlation between the degree of edema and serum albumin concentration, as well as the rise in the serum albumin values as edema regressed would support the fact that there is a causal relationship between nutritional edema and serum albumin concentrations . However since serum albumin level did not reverse back to the normal range after edema had clinically and anthropometrically disappeared would support the fact that other factors besides hypoalbuminemia woud contribute to the pathogenesis and regression of edema .

Kidney malfunction rather than hypoalbuminemia has been postulated as the primary cause of edema in kwashiorkor, ( Khar and Alleyene, 1973 ), while potassium deficiency is said to be responsible for renal malfunction

( Mann et al., 1972 ) .

Other suggested factors responsible for edema include increased mineralocorticoid, glucocorticoid, renin, A. D. H activities, ( Srikantia and Mohanranm, 1970 )

Unfortunately, renal hemodynamics, activities of the previous hormones have been shown to be identical in edematous and non edematous cases of severe malnutrition ( Laditan and Reeds, 1976 )

In a study done by Ahmed et al., ( 1988) on rats fed different diets containing different amount of proteins, it was found that malnutrition causes functional thiamine deficiency . Yet in a study done on wet beriberi, edema was a constant finding in all cases and this edema subsides upon treatment with thiamine ( Tanphaichitr et al., 1970 )

However, none of the previously mentioned studies showed the effect played by thiamine in pathogenesis of edema in protein energy malnutrition .

## *Aim of the work :*

This work aims at studying the role played by thiamine in pathogenesis of edema as a contributing factor to other etiological agents in cases of protein energy malnutrition .

# *REVIEW OF LITERATURE*

# Thiamine

Vitamins are organic substances occuring in natural food as such or as precursors, which are reqiured by the animal organism in minute amounts for normal growth and health . They can't be synthesized in the body by anabolic reactions ( Rashid, 1991 ) .

Thiamine consists of a substituted pyrimidine Joined by a methylene bridge to a substituted thiazole (Martin, 1981 ) .

## Properties :

Thiamine is basic due to the amino group at $c_4$ of the pyrimidine ring and N - 3 of the thiazole ring. It is generally prepared as a chloride - hydro, soluble in water and 90% ethanol but not in fat solvents . In this form - it is acid in aqueous solution owing to dissociation of the Hcl, it is rather resistant to heat( boiling or autoclaving ) , in solutions below PH 3.5, but loses activity above pH 5.5 (hydrolysis ) . The relative stability of thiamine in foods, under ordinary conditions of preparation, may be due to the fact that much of it is in combined form . However, the high solubility may result in considerable loss in the cooking water (Cantarow, and Schepartz, 1967) .

The vertue of its basic characters, it forms a number of salts and esters which possess equal vitamin activity on a molar basis. The most important ester is the pyrophosphate ( reacting with the alcoholic - OH on the thiazole ring ) which serves as the prosthetic group (carboxylase ) for metabolic reactions involving decarboxylation of $\alpha$ - keto acids and for the transketolase reaction .Thiamine and its pyrophosphate undergo both oxidation and reduction. Treatment in vitro with mild oxidizing reagents (e.g potassium ferricyanide ) results in the formation of thiochrome. The reaction forms the basis of one of the methods for quantitative determination of thiamine. Reduction (e.g hydrosulfite ) results in irreversible loss of vitamin activity (Cantarow, and Schepartz,1967) .

## *Biosynthesis and source of thiamine :*

Thiamine is a nutritional requirement for all plant and animal species . It is synthesized by all higher plants, but to only a limited extent in the dark and by many bacteria, yeasts and molds . Certain plants and microorganisms can synthesize thiamine if the pyrimidine component alone is supplied, while others require neither of these components in a preformed state .

***The final steps in the synthesis involve :***

a - Coupling of the pyrimidine and thiazole monophosphate (methylene bridge ) .

b - Hydrolysis of the latter, forming the free base (thiamine) ;

c - Pyrophosphorylation of the latter with ATP, forming thiamine pyrophosphate. Cocarboxylase activity is exhibited by thiamine pyrophosphate, not by the free base. Cells of several tissues contain enzymes capable of phosphorylating thiamine in the presence of ATP, or if coupled with enzymatic reations in which reactive phosphate compounds are formed . **(Cantarow,and Schepartz, 1967 )** .

Thiamine is present in almost all plant and animal tissues, commonly used as food, but the content is usualy small **(Martin,1981)** .

Thiamine occurs in highest concentration usualy in the seed, but also in the leaf, root, stem and fruit . In cereal grains, it is concentrated in the outer germ and bran layers (e.g rice polishings) which are often discarded during milling processes (e.g wheat flowr and rice). The following are good dietary sources of this vitamin : peas, beans, whole cereal grains, bran, nuts, prunes, goosberies, skilled yeast, whole wheat bread is a good source; white bread is now commonly made from thiamine enriched flour, and is therefore satisfactory from this standpoint . Thiamine is present in most animal tissues. Of those which are commonly used as foods, ham and pork, beef, liver, eggs also supplying considerable amounts . Milk, although containing comparatively low concentrations, is an important dietary source because of the large quantities consumed . Cow's milk contains about 40 μg./dl and human milk 16 μg./dl, in contrast to the richer sources listed above which typically provide 400 µg./100gr. Nevertheless, breast fed infants do not develop thiamine deficiency provided that their mothers are not themselves deficient . The toxicity of thiamine is low so that no upper limit of advisable intake is required ( Cantarow, and Schepartz, 1967 )

## *Metabolism of thiamine :*

Free thiamine is absorbed readily from the small intestine, but the pyrophosphate (co - carboxylase ) is not . The bulk of the dietary vegetable thiamine is in the free state. It is actively phosphorylated to cocarboxylase in the liver and, to a lesser extent in other tissues ( muscle, brain ) including nucleated red blood cells . It is present in the blood plasma and cerebrospinal fluid in the free state (about1ug / 100 ml) The largest portion of the blood thiamine is in the blood cells as the pyrophosphate, in protein combination. Since free thiamine (Base) is readily diffusible and the pyrophosphate is not, the plasma thiamine probably represents the transport form (inactive) of the vitamin, which undergoes phosphorylation upon entrance into tissue cells including nucleated red blood cells in the bone marrow . ( Cantarow, and Schepartz, 1967 )

The capacity of the organism for storing thiamine is limited . It is present in both free and combined forms, mainly the latter, in the heart,liver, and kidneys, and, in lower concentration in skeletal muscle and brain. Administration of thiamine may result in an increase in the tissues, within certain limits .However, on a thiamine free diet, the tissue content is depleted within a short time, emphasizing the desirability of providing an adequate daily supply .

( Cantarow, and Schepartz, 1967 )

Cocarboxylase, formed within the cell, unites with protein apoenzymes to form carboxylase, one of which (pyruvic carboxylase ) contains magnesium. The pyrophosphate group is apparently involved in this union the pyrophosphate linkage in cocarboxylase is readily hydrolyzed by tissue pyrophosphatases, free thiamine being liberated. However when the coenzyme is combined with the apoenzyme it is quite resistant to such hydrolysis, thiamine is released from this combination through the action of proteolytic enzymes .