A COMPARATIVE STUDY OF LIVER FUNCTIONS IN PROTEIN ENERGY MALNOURISHED EGYPTIAN INFANTS AND CHILDREN

THESIS

Submitted in the Partial fulfilment
for the degree of M. Sc.
(Pediatrics)

BY

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1978

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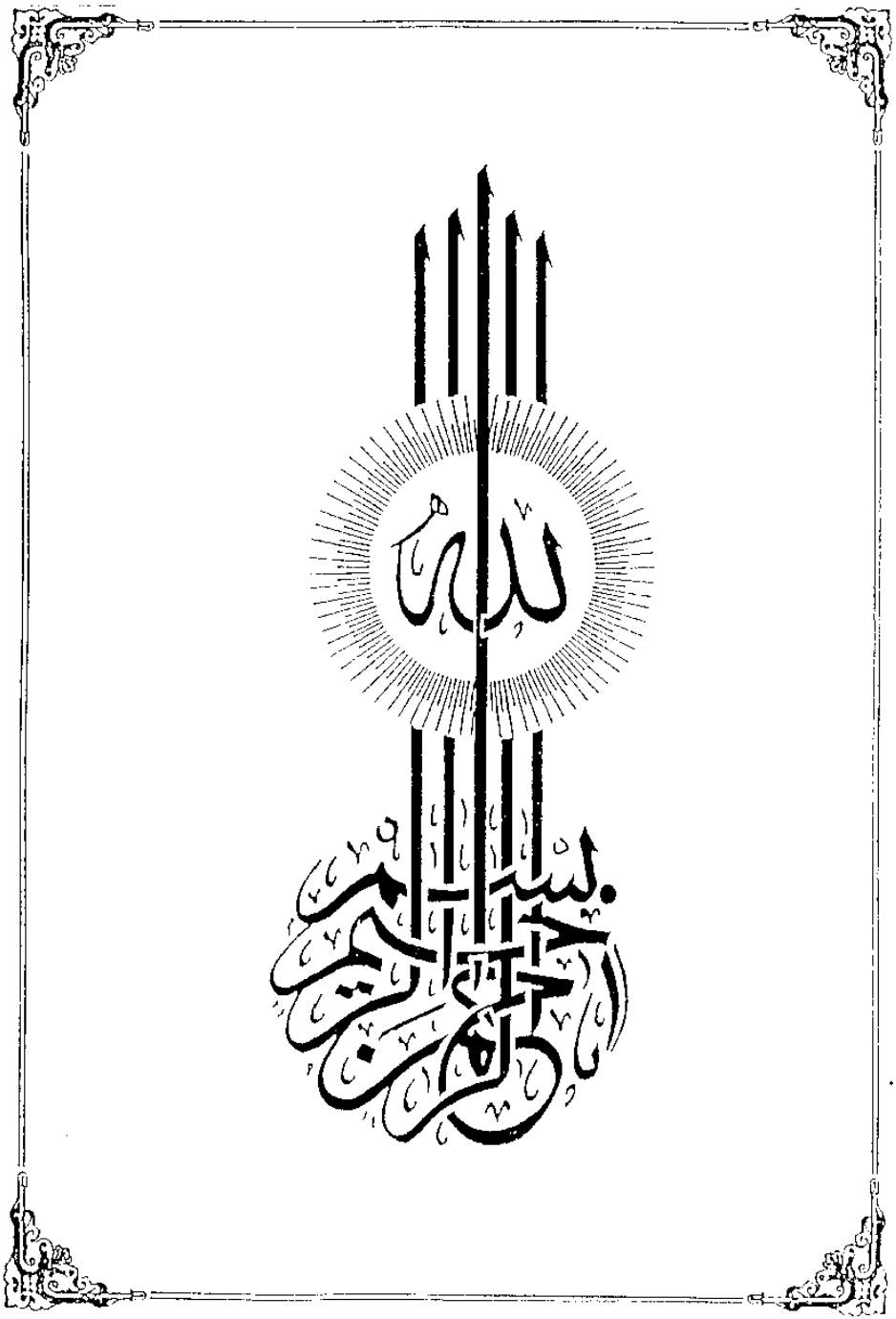

INTRODUCTION

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Protein energy malnutrition (P.E.M.) is one of the main health problems in the developing countries and in the age group below 5 years this problem has grave dimensions[1].

Although this disease has long been known by paediatricians all over the world and is considered a well established clinical and pathological entity, yet only few attempts have been made to clarify some of its many obscure aspects by the use of more advanced and sensitive methods of investigations.

These facts stimulated us to study some aspects of this disease in more details as a better understanding of the biochemical and pathological lesions occuring in the different organs in this condition may help a great deal in opening new fields of prevention and treatment.

The affection of the liver in nearly almost all of the nutritional disorders stimulated us to carry out in this study some of the important liver functions and histopathological changes in cases of P.E.M. namely marasmus, kwashiorkor and marasmic kwashiorkor.

REVIEW OF LITERATURE

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A balanced diet should have certain proportions of nutrients and calories. If the proportions are balanced to meet the physiological requirements and the diet is fed in adequate amount, normal nutrition results (Eutrophy). If the diet is well balanced but is inadequate in amount the disease process is called "undernutrion", but if the diet is not well balanced, then "Malnutrition" occurs even if this poorly balanced diet is fed in amounts adequate to supply hunger. Dystrophy implies failure of normal growth due to undernutrition or malnutrition[1].

Surveys carried out in many developing countries including Egypt have shown that the milder forms of energy protein malnutrition (E.P.M.) represent 50% - 80% of the child hood population under 5 years of age, while the severe forms are around 10%[2].

To define early E.P.M. we should refer to the classification recommended in 1970 by the Wellcome International Survey in Jamica[3] which is simple and satisfactory from the clinical and

research points of view. Weight less than 60% of the standard without aedema is equivalent to marasmas, weight less than 60% of the standard with aedema is equivalent to marasmic kwashiorkor, weight from 60 - 80% of the standard with aedema is equivalent to kwashiorkor, weight from 60 - 80% of standard without aedema is equivalent to simple underweight or early E.P.M., weight more than 80% of the standard is considered a healthy child.

Lack of nutrition as a primary cause is one of the most important factors. Deficient breast milk during early infancy is the most important factor, in addition to the poor quality of supplementary foods as a result of poverty and ignorance. It was shown also that P.E.M. is always associated with multiple deficiencies of several vitamins and minerals and not mere protein and calorie deficiency(10). Parentral infections and repeated attacks of acute infection resulting in diarrhea and vomiting, play a considerable precipitating factor(11). The severity and acuteness of underfeeding are also important in deciding why a child would develop marasmas and another one develops kwashiorkor. This

was explained by Gopalan in his adaptation theory[13]. Hypocaloric dwarfism and marasmas probably represent states of appropriate adaption to conserve life and vital functions particularly those of the C.N.S. and liver, at the expense of growth and function in another tissues. Kwashiorkor probably represents failure of adaptation or decompensation of a previously appropriate adaptation[17].

The age incidence of P.E.M. tends to be at an increasingly early age in many parts of the world (14). It was found in the nutrition clinic of Cairo University Pediatric Hospital that the frequency of Kwashiorkor in the early months of life (2-3 months) had been increasing (15).

P.E.M. is a prevalent disease among poor classes in Egypt. When the body fails to receive its proper nutritive requirements, it is forced to draw upon its own tissues for maintenance. The stored glycogen and fat are burned in preference to proteins, but when the fat and carbohydrate stores are exhausted a general consumption of protoplasm occurs[16].

In Kwashiorkor, the clinical signs may be preceded by some months of delayed and eventually arrested growth. But this prodromal phase is usually shorter than with marasmas. The clinical features are divided by Jelliffe (1968) into 3 groups: Constant: aedema, growth failure, muscle wasting with some retention of subcutaneous fat, irritability and listlessness, Usual: sparse, depigmented, friable hair, light coloured skin, moon face, moderate aedema and loose stools, occasional : flaky paint dermatitis, hepatomegaly, skin ulcers, fissures and blisters, associated vitamin deficiencies varying with the local dietry pattern and infection[12].

The constant features in marasmus include growth retardation and wasting of the muscles and subcutaneous fat. Occasional features include vitamin deficiencies and infection. In contrast to kwashirkor loss of appetite is uncommon.

The most marked pathological changes in P.E.M. are excessive fat deposition within liver and atrophy of the pancreas but most organs show some changes.

Kwashiorkor has been studied in much greater detail than marasmus, probably because it is a more clinically obvious disease.

Fatty infiltration of the liver is found in almost all children with clinical signs of kwashiorkor; marasmic children without hair or skin changes usually have normal livers (Waterlow, 1948; Trawell et al, 1954).

Atrophy of the pancreas particularly of the acinar cells figured prominently in early description of the pathology of kwashiorkor (Thompson Trowell 1952, Trowell et al 1954). Marasmic children showed evidence of pancreatic deficiency when the plasma albumin was below 3 gm per 100 ml (Burbezat and Hansen 1967).

Other pathological changes in most organs were associated specially in gastrointestinal tract showing varying degrees of villous atrophy (33). Outside the gastrointestinal tract changes include reduced osteoblastic activity (Doe et al 1965), abnormalities of cardiac and skeletal muscles (Chauken et al 1965) hyalinization of glomeruli and fatty degeneration of convoluted tubules of kidneys (33).

Atrophy of thymus gland and lymphoid tissue (33) atrophy and keratosis in the skin similar to dermatitis of pellagra (33). In general organs with a high protein turnover are affected first but most changes are reversible (Ramalingaswami and Doe 1968) Infection and anaemia are common (33).

The general consumption of protoplasm is usually reflected on serum contents as proteins (4), lipids (5), carbohydrates (6), enzymes (7) and electrolytes (8) leading to various changes.

In mild kwashiorkor plasma esterified cholesterol (E.Ch) and phospholipid (P.L.) values were normal, where as, those of total cholesterol (T.Ch., Free cholesterol (F.Ch) and total lipids (T.L.) were slightly significantly elevated. In moderate and in particular severe kwashiorkor highly significant drop in plasma T.L., P.L., T.Ch. and especially E.Ch. were demonstrated. Decrements in E.Ch were proportional to the severity of the condition plasma E.Ch. was normal and slightly lowered in moderate and severe kwashiorkor respectively (34).

Marasmic children also have (Haden 1969) raised F.F.A. and triglycerides initially but the other serum lipids are normal.

Total serum protein concentration is always reduced (35). This is mainly due to hypoalbuminemia which is a basic change in kwashiorkor and to some degree in marasmas. The alpha 1 and alpha 2 globulins have been found to be relatively increased and the Beta globulins frequently decreased. The gamma globulin serum concentration is variable but always high when expressed per unit of total serum protein. Those serum protein alterations and impaired hepatic circulation are belevied to be responsible for abnormal flocculation and turbidity liver function tests and high B.S.P.

The pathological studies in kwashiorkor revealed that the main pathological features show fatty infiltration of liver cells which starts centrilobular and spreads peripherally. Cell necrosis and degeneration occur in severe cases (19). First it was beleived that the fatty change is a constant and early finding (20). However, the experience of

many workers has been different, and the abscence of fatty change in a quite considerable number of cases had been found (21.22). It was also shown by some workers (9) that the fatty change although a common finding in most cases, was not constant neither in the liver biopsy material nor in the liver of fatal kwashiorkor. Other forms of liver injury as cytoplasmic vacuolation, reduction of cytoplasmic basophilia and necrosis have been recognized as well, both in kwashiorkior and in experimentally induced similar conditions (22, 23).

Again the problem of complicating cirrhosis has been also controversal. Gillman 1945[24] in his report of south African cases had found in 12.5% frank pigmentary cirrhosis, in 20% pre-cirrhotic changes and in 30% there were signs of serious hepatic damage amounting to cirrhosis.
Shanda in 1958[25] in a report of 34 P.M. cases of indian kwashiorkor stressed the evolution of cirrhosis from the fatty change and reported pre-cirrhotic changes in 8 cases, poot infiltration cirrhosis in 4 cases and post necrotic cirrhosis in one case .

In 1964[9] some workers found only mere thickening of the portal tracts by round cell infiltration in most cases and together with fibroblastic proliferation which advances only in very few cases to surround the lobules and give a simulation of monolobular cirrhosis. In only one case of 15 P.M. cases they found true mesenchymal irritation and proliferation of the intralobular reticulum to segregate liver cell groups. They were of the opinion that the false monolobular pattern occasionally seen in kwashiorkor cannot be considered a state or even a stage in the process of cirrhotic transformation.

The liver is the largest gland in the body and performs a large number of functions many of which are essential to life (27).

The metabolic function is the most important and it has a role in protein, fat and carbohydrate metabolisms. As regards the role of the liver in protein metabolism, the greater part of plasma is made in the liver, the albumin, some of globulins (alpha and beta) and also several factors concerned in coagulation (27). Liver function tests may be classified according to the various functions