ASSESSMENT OF SERUM LIPIDS IN EGYPTIAN INFANTS & CHILDREN SUFFERING OF HEPATOMEGALY

THESIS

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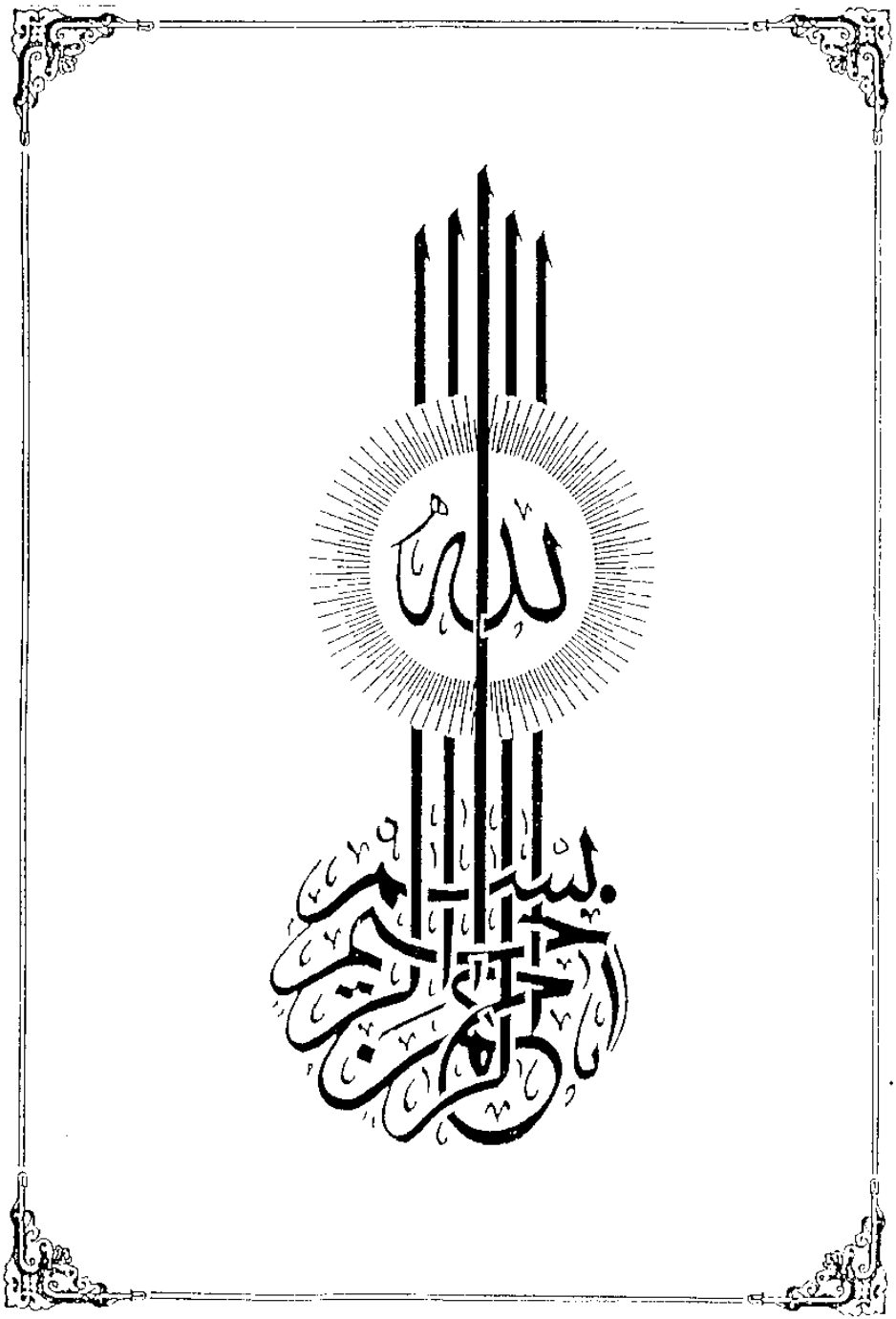

C O N T E N T S

INTRODUCTION

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The liver is one of the key organs in the metabolism of lipids in the body.

Under normal conditions most of the fatty acids taken up by the liver, and esterified to triglyceride, are derived from adipose tissue or the diet. Some fatty acids (especially saturated ones) are synthesized in the liver from acetate. The fatty acids may then be converted enzymatically to triglyceride, esterified with cholesterol, incorporated into phospholipids or oxidized to CO_2 or ketone bodies. Most of the triglycerides is produced for export and in order to be secreted must be converted to lipoproteins by combining with relatively specific apoprotein moieties. Thus the protein synthesis is important for the release and secretion of triglycerides from the liver *(Shafritz et al., 1981)*.

Hepatomegaly is a physical finding which may suggest either, intrinsic liver disease or may represent a more generalised disorder *(Walker and Mathis, 1975)*.

Alterations of plasma lipid distribution in patients with cholestasis had been recognized for a long time *(Ruse et al., 1956 & Switzer, 1967)*. *Man et al. (1945)* found an abnormal lipid profile in cases with hepatic biliary obstruction characterized by a predominant elevation in phospholipids

and a less pronounced rise in cholesterol and triglycerides. In acute hepatitis, disorders of lipid metabolism were studied by some workers. *Mendenhall and Mortiaux (1962)* reported an increase in plasma triglycerides and free fatty acids. *Sherlock (1968),* found that serum cholesterol particularly in its esterified form, was reduced in hepatitis cases. Increased beta-lipoproteins and alpha-lipoproteins were found by other investigators *(Papadopoulos and Charles, 1970 & Kindnmarch and Lourel, 1972)*. Hepatocyte fat accumulation can occur in protein-calorie malnutrition (KWO) as a result of inadequate synthesis of lipoproteins and consequent decrease in pinocytic transport of lipid from hepatocyte *(Alpers and Sabesin, 1982)*.

AIM OF WORK

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The aim of the present work was to study the changes in lipid metabolism in different cases of hepatomegaly in Egyptian infants and children compared with normal controls of the same age and living under nearly the same circumstances. This may delineate the significance of dietary regimen free of fats in cases of liver disease.

REVIEW OF LITERATURE

PART I

LIVER AND LIPID METABOLISM

L I P I D S

Lipids are important dietary constituents not only because of their high energy value but also because of fat soluble vitamins and essential fatty acids which are found with fat of natural foods *(Harper, 1977)*.

In the body, fat serves as an efficient source of energy both directly and potentially, when stored in adipose tissue. It serves as an insulating material in the subcutaneous tissues and around certain organs. The fat content of nerve tissue is particularly high *(Curr and James, 1975)*.

Combinations of fat and protein (lipoproteins)are important cellular constituents, occurring both in the cell membrane and in the mitochondria within the cytoplasm and serving also as the means of transport of lipids in the blood *(Felts et al., 1975)*.

PLASMA LIPIDS

The major lipids in plasma do not circulate in the free form. Free fatty acids are bound to albumin, whearas cholesterol, triglycerides and phospholipids are transported in the form of lipoprotein complexes *(Lioyd and Fosbrooks, 1974)*. There are five families of lipoprotein which are graded in size and lipid content. The density of these lipoproteins

and consequently the speed at which they sediment in ultra-centrifuge is inversely proportionate to their lipid content *(Ganong, 1983)*.

A) Chylomicrons: They are formed in the intestinal mucosa during the absorption of long chain fatty acids into the lymphatic ducts. Their size varies from 800-1000 A^{o} *(Felig et al.,1981)*. After meals there are so many of these large particles in the blood that the plasma may have a milky appearance (Lipemia). The chylomicrons are cleared from the circulation by the action of lipoprotein lipase *(Azizi et al., 1978)*. This enzyme catalyzes the breakdown of the triglyceride in the chylomicrons to free fatty acid and glycerol which then enter the adipocyte and are re-esterified. The remanants of the chylomicrons are metabolised in the liver *(Levy et al, 1974)*.

B) Very low density lipoproteins (VLDL): are principally formed in the liver and they are in turn converted to

C) Intermediate density lipoprotein (IDL) and low density lipoproteins (LDL) by loss of some triglycerides and protein in the complexes *(Ganong, 1983)*. VLDL are the

major transport vehicles for endogenous triglycerides in plasma and are of smaller size than chylomicrons and range in diameter from 300-800 A^{o} *(Felig et al., 1981).*

D) Low density lipoproteins: are the principal carriers of cholesterol in the circulation and play an important role in cholesterol metabolism. They attach to receptors on the surface of many cells in the body and are ingested into the cell by endocytosis. In the cell lysosomal enzymes breakdown the protein leaving the lipid free for incorporation into membranes or other uses *(Harper, 1977 and Ganong, 1983).* *Felig et al.,(1981)* reported that LDL molecule is composed of 25 per cent protein and 75 per cent lipid.

H) High density lipoproteins (HDL) are formed in the liver *(Ganong, 1983).* They are the heaviest and smallest diameter (90-120A^{o}) of human lipoproteins and contain about equal proportions of lipids and proteins *(Felig et al., 1981).*

The HDL are often called "alpha" lipoproteins on the basis of their electrophoretic mobility; the LDL and VLDL are often collectively called "beta" lipoproteins, although strictly speaking they do not uniformly have B mobility on electrophoresis *(Switzer, 1967).*