STUDY OF SERUM LEVELS OF HIGH DENSITY LIPOPROTEIN – CHOLESTEROL IN SCHISTOSOMAL HEPATIC FIBROSIS

Thesis Submitted in Partial Fulfilment
for the Master Degree
in
General Medicine

By
Anwar Shafik Faltas
M. B., B. Ch.

Supervised By

Prof. Dr. ADEL SHAKER
Professor of
General Medicine

Prof. Dr. M. SABRY SALLAM
Ass. Professor of
Clinical Pathology

Prof. Dr. M. ABDEL FATTAH TAHA
Ass. Professor of General Medicine

Faculty of Medicine
Ain Shams University

1983

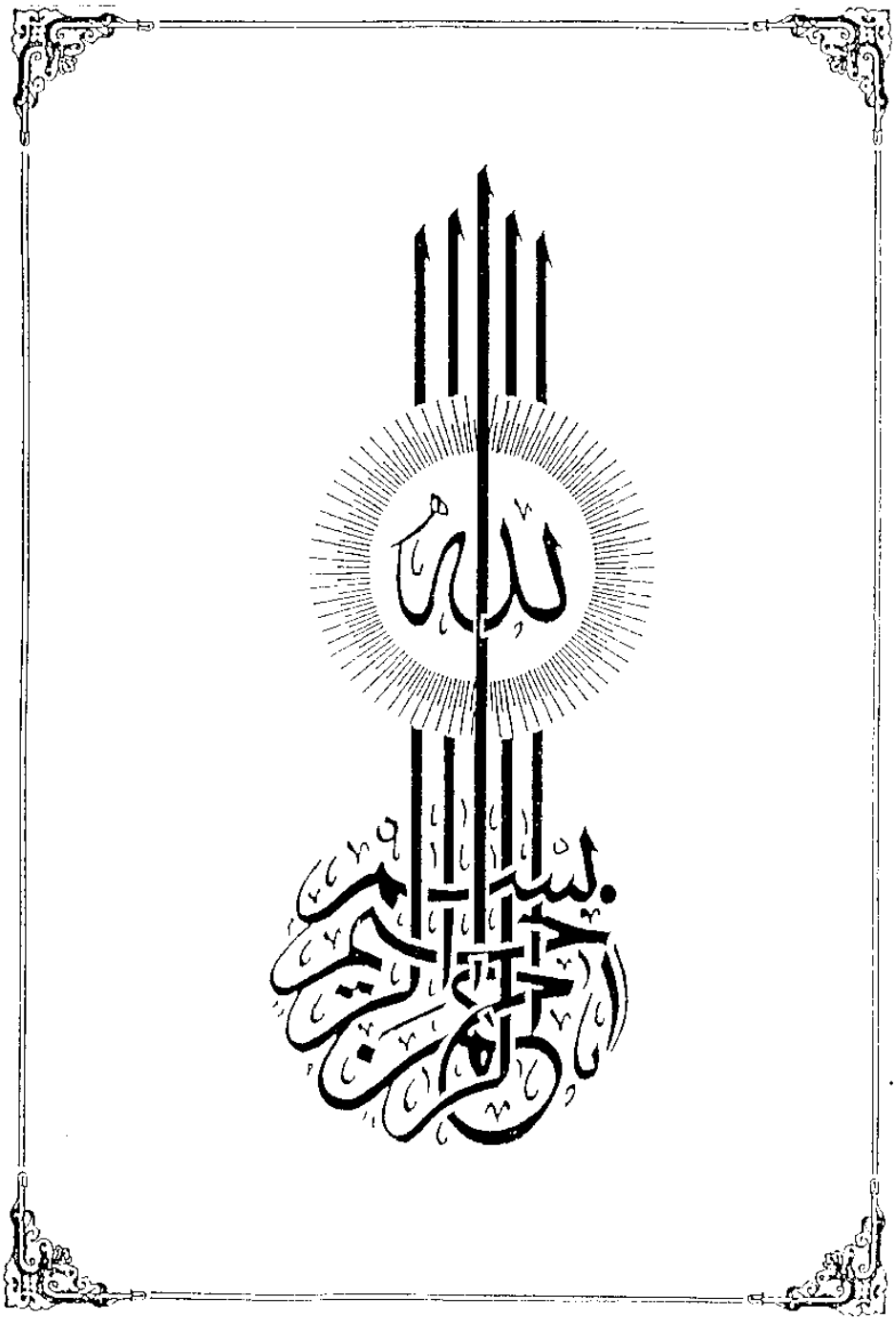
ACKNOWLEDGEMENT

I am greatly honoured to express my feelings of sincere gratitude and utmost thanks to Professor Dr. ADEL SHAKER , for his goodness and kindness. He spent a lot of his valuable time in meticulously revising, advising and helping in all parts of this work . He was continuously encouraging and guiding me, and his expert advice could lead me to proceed in this work up to its end .

I wish to record my great indebtedness and gratitude to Professor Dr. M. SABRY SALLAM, for he offered much of his time and experience in providing me with advice, suggestion and planning for the work. He generously allowed me to work in the lab. of the protein chemistry unit and was always supervising the practical work very accurately.

It is a great pleasure to record my overlasting gratitude and thankfulness to Professor Dr. M. ABDEL FATTAH TAHA for his fine touches and valuable notes which helped me so much in collecting the scientific material and writing the review . He also helped me in performing the statistical analyses of the collected results .

I am deeply thankful to Dr. HAMZADA IBRAHIM, Dr. NADIA NAGUI, Dr. NAZEK KAMAL and Dr. GIHAN KAMAL for they generously and



friendly spent a lot of their time in making the electrophoresis and protein estimations. They were always beside me in the lab. and they willingly gave me their valuable experience in the lab. work which helped me so much in my practical work .

CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION
AND
AIM OF THE WORK

INTRODUCTION AND AIM OF WORK

The subject of high density lipoprotein-Cholesterol (HDL-Cholesterol) and the relation of its levels in serum to ischaemic heart disease,has gained great interest. It is widely investigated nowadays and an inverse relationship has been found between the level of HDL-Cholesterol and the incidence of coronary heart disease(Castelli,W.P., et al,1977(a), Gordon, T., et al,1977 and Jenkins, P.J., et al,1978).

The interest in the study of HDL-Cholesterol has expanded to discover the relation of its levels in serum with many other diseases and it has been found that HDL-Cholesterol concentrations were lower in patients with maturity-onset diabetes mellitus than in those with juvenile-onset diabetes mellitus (Kennedy,A.L., et al,1978).

In addition, the levels of high density lipoproteins (HDLs) have been investigated in cases of chronic renal failure (Savdie, E., et al,1979) and in cases of peripheral vascular disease (Zilcher, H., et al,1979).

Many studies were done to estimate the levels of lipoproteins in liver diseases and it has been reported that in parenchymal liver diseases, there are certain changesin serum

lipids, in the electrophoretic pattern of lipoproteins (Papadopoulos, N.M., et al,1970, Devi,C.S., et al,1976 , Kajiyama, G., et al,1981 (b) and Takagi,Y.,1980) and an abnormal composition and morphology of high density lipoproteins (Frote, T., et al,1974).

Alterations in serum lipoproteins in chronic parenchymal liver diseases are similar to those of acute liver injury but are less striking. So, lipoprotein abnormalities when seen in chronic liver diseases, probably reflect continuing hepatic injury (Turner, K.B., et al,1953 and Papadopoulos,N.M.,et al, 1970).

In cholestasis, most of lipoprotein disturbances arise as a result of secondary hepatocellular dysfunction but there is one abnormality which appears to be primarily the result of biliary stasis; the presence of an abnormal lipoprotein which is called lipoprotein-X (Ritland, S., et al,1975) .

Schistosomiasis is one of the most important worm infestations of mankind. It is widely distributed over three continents affecting more than 200 million people and is often associated with considerable morbidity.

It is increasing in prevalence as man attempts to use water and land resources more efficiently with construction of new dams and initiation of irrigation projects which provide ideal breeding places for the snail host of the parasite. Schistosomiasis is therefore a challenge not only for physicians and scientists, but also for water engineers, economists and politicians (Mahmoud,A.A.,1977).

Schistosomal hepatic fibrosis is fairly common in Egypt and it causes incapacitation to a great number of farmers .

Some authors investigated the serum lipid pattern in Schistosomal hepatic fibrosis (Mousa, A.H., et al,1967 , Ghanem,M.H., et al,1971, Mousa,W., et al,1975 and Gillet , M.P.T., et al,1976) and few others have reported that this disease alters the electrophoretic pattern of lipoproteins and their levels in serum (El-Kharbotly,M., et al,1965, Gillet , M.P.T., et al,1978, Cechirel,Y.M., et al,1978 and Owen , J.S., et al,1978).

To our knowledge,the serum levels of HDL-Cholesterol have not yet been studied in cases of Schistosomal hepatic fibrosis. So, it has been thought that studying the serum level of HDL-Cholesterol in this important group of Egyptian patients, may add a valuable datum to the literature .

REVIEW OF LITERATURE

REVIEW OF LITERATURE

PLASMA LIPIDS

Extraction of plasma lipids with a lipid solvent and separation of the extracts into various classes of lipids shows the presence of : -

I. Triglycerides (Triacylglycerols): -

They may be derived from diet (exogenous)or synthesized in the liver (endogenous).

The exogenous triglycerides are synthesized in the intestine, carried by lymphatics as chylomicrons and poured into the circulation via the thoracic duct, they normally occur in the serum in the post absorptive period only and disappear within 10-12 hours .

The endogenous triglycerides are synthesized by the liver where they are incorporated into very low density lipoproteins (VLDL) and are present even in the fasting state .

The normal concentration of triglycerides in plasma in the fasting state is 65-165 mg/dl .

Triglycerides(Triacylglycerols) are continually hydrolyzed and resynthesized in the adipose tissues in an equilibrium state in normal conditions. Hydrolysis is catalyzed by

hormone-sensitive lipase to : Free Fatty Acids and Glycerol. However, adipose tissues lack the necessary enzyme for resynthesis of triglycerides from glycerol, instead, the free fatty acids are combined with α-glycerophosphate which is derived from intracellular glycolysis i.e. carbohydrate metabolism to resynthesize the triglycerides. So, the most crucial factor in this reaction is the availability of intracellular glucose. (Mayes, P.A., 1981.(a)) .

II. Phospholipids :

They are widely distributed in all tissues and are major constituents of biological membranes. In bile, phospholipids are important in keeping cholesterol in solution and in the lung, lecithin is an essential component of surfactant . Dietary phospholipids may be absorbed as such because of their relative solubility but the phospholipids of plasma are derived mainly through synthesis in the liver and their normal range is 123-390 mg/dl. Lecithin forms the main fraction of them (50-200 mg/dl.) and plasma lecithin is the source of fatty acids for esterification of cholesterol in alpha lipoproteins and being hydrophobic molecules, they are important components of almost all the lipoprotein fractions especially high-density lipoproteins(HDL), Low-density lipoproteins (LDL) and very low-density lipoproteins(VLDL)(Cantarow and Trumper, 1975).

III. Cholesterol : -

It is both absorbed from the gut and synthesized in the body. Absorption is largely proportional to intake . To a certain extent, high intakes are compensated by reduced endogenous synthesis but this is not complete and plasma cholesterol values are usually higher with a high cholesterol intake than with a low one and the nature of fat in the diet influences plasma cholesterol levels :

Saturated fatty acids found in animal fats increase plasma levels while polyunsaturated fatty acids found in vegetable oils, tend to lower them. Cholesterol in the gut is absorbed after incorporation in mixed micelles and bile salts are necessary for this process. In the intestinal mucosa, the absorbed cholesterol is esterified and transported in the lymph in chylomicrons and pre-beta lipoproteins synthesized in the intestinal wall (Zilva, J.F., et al,1975).

Most tissues of the body particularly the liver and small intestine synthesize cholesterol from acetyl Co A. Cholesterol released from the peripheral tissues is taken up and esterified (with a fatty acid from lecithin by the enzyme lecithin cholesterol acyl transferase (LCAT)) in alpha lipoproteins and transferred to beta lipoproteins where most of the plasma cholesterol is found. About two thirds is esterified .