A STUDY OF LIPOPROTEIN (a) SERUM LEVEL AS AN INDEPENDENT RISK FACTOR AND ITS ASSOCIATION WITH CORONARY HEART DISEASE

THESIS SUBMITTED FOR PARTIAL FULFILMENT OF
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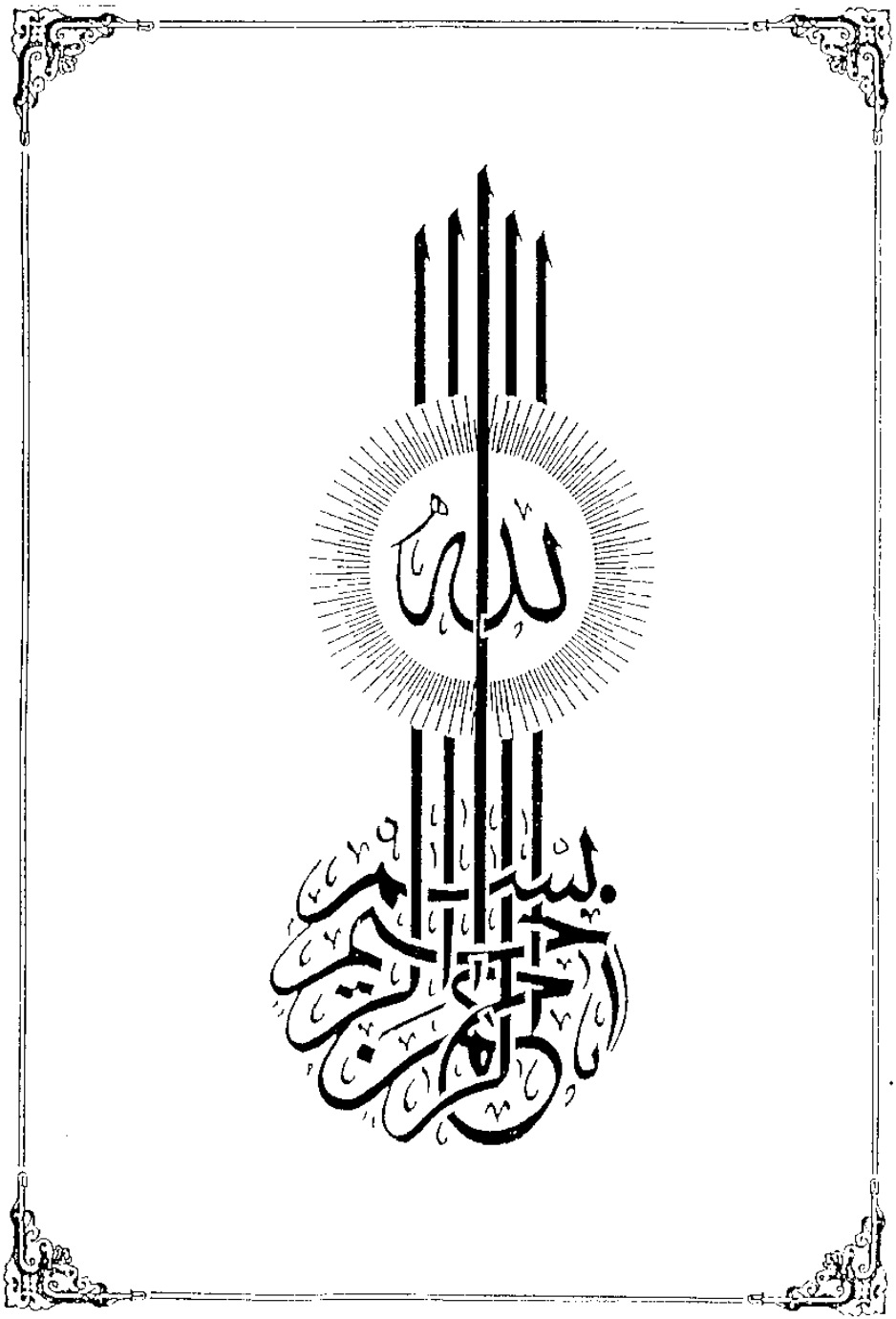

TO MY FAMILY

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INTRODUCTION & AIM OF THE WORK

INTRODUCTION

Lipoprotein (a) "Lp (a)" is a cholesterol-rich plasma lipoprotein with pre-B mobility in lipoprotein electrophoresis. Its lipid composition is similar to that of low density lipoproteins (LDL), but the protein composition is different, consisting of two major proteins, apo B 100 and apo (a) linked by a disulfide bridge.

Recently, Lp(a) has attracted interest because several studies have shown that high concentrations of Lp(a) are associated with atherosclerosis, cardiovascular diseases, myocardial infarction and cerebrovascular accidents.

Its concentration in serum is largely determined by heredity and seems insensitive to either diet, lifestyle or drugs.

The atherogenecity of Lp(a) either originates from its role in lipid metabolism or through inhibiting fibrinolysis by reducing the generation of plasmin.

AIM OF THE WORK

The aim of this work is to find the association between Lp(a) and the development of coronary atherosclerosis, to assess the relation between Lp(a) and the extent and severity of coronary artery disease and finally to study the correlation of Lp(a) with the other lipid and lipoprotein parameters.

Review of Literature

CHAPTER I

SERUM LIPIDS, LIPOPROTEINS AND APOLIPOPROTEINS

I- Lipids

Lipids are natural products that are not soluble in water (aqueous media) but are readily soluble in organic solvents such as alcohol, chloroform, hexane and diethyl ether. There are four major classes of lipids namely, sterols (cholesterol), triglycerides, phospholipids, and fatty acids ***(Stein, 1987).***

A) Cholesterol:

In man, cholesterol is present in all body tissues and most cells can synthesize cholesterol. It is present in two forms : the free hydroxyl form and as cholesteryl ester. Serum and biological specimens contain a higher percentage of cholesterol esters (75 % - 85 %) than free cholesterol (15 % - 25%). Cholesterol is one of the major constituents of cell membrane. Cellular membranes control the flow of water soluble products in and out of cells and lipids help to serve this function because of their limited solubility in water ***(Steinberg et al., 1987).***

The other major function of cholesterol is being a metabolic precursor for other steroids as female and male sex steroids (estrogens and androgens), adrenal steroids (aldosterone and corticosterone), and bile acids ***(Schaefer et al., 1982)***

B) Triglycerides:

These compounds are derived from mixtures of long - chain fatty acids esterified to glycerol. Triglycerides are the primary constituents used for long term energy storage. Thus, their metabolism is the key component of man's ability to store and derive energy for many of the body's functions ***(Stavropoulous and Crouch, 1974 and Mahley et al., 1984).***

C) Phospholipids:

Phospholipids are structurally similar to triglycerides. They are major components of cell membranes and also act in solution to alter fluid surface tension (e.g. surfactant activity of the fluid in the lungs) ***(Stein, 1987).***

D) Fatty acids:

Nonesterified free fatty acids are a minor constituent in circulating plasma lipids or tissue stores. However, they are an integral part of most lipids through ester bonds. The primary physiologic function of long chain fatty acids is to provide energy to cells and muscle tissue by an oxidative process referred to as β- oxidation ***(Stein, 1987).***

II- Lipoproteins and their Classes

Lipoproteins are composites of lipid and protein that provide solubility characteristics in aqueous media that enable lipid movement and metabolism ***(Osborne and Brewer, 1977).***

Lipoproteins are spherical in shape with neutral lipid (triglycerides and cholesterol esters) at the center surrounded by free cholesterol, together with phospholipids, and proteins on the surface. Specific proteins (apolipoproteins) are associated with lipoproteins that have both hydrophilic and hydrophobic characteristics, such that part of the apolipoprotein prefers an aqueous environment while the other portion wants to interact with lipid material ***(Scanu and Landsberger, 1980).***

Plasma lipoproteins were first separated and named according to their electrophoretic migration on solid support media, into those remaining at the origin (chylomicrons), prebeta, beta and alpha migrating species. They were also classified on the basis of particle size, or most commonly according to sequential ultracentrifugal flotation into 5 major classes: Chylomicrons, very low density lipoproteins (VLDL), intermediate density lipoproteins (IDL), low density lipoproteins (LDL).and high density lipoproteins ***(Patsch et al., 1974, Carlson and Ericsson, 1975 and Mahley et al., 1984). Table (1)***

TABLE (1) SUMMARY OF LIPOPROTEIN PROPERTIES *(ONAKA, 1993)*

	Chylomicrons	*VLDL*	*LDL*	*HDL*
Electrophoretic mobility	None	Pre-beta	Beta	Alpha
Size (A°)	750-12.000	280-750	215-220	65-95
Protein content	2.5%-5%	7.1%	20.7%	50%
Phospholipid content	7.1%	26%	20%	21.9%
Triglyceride content	81.3%	51.8%	9.3%	8.1%
Cholesterol content	9.1%	22.2%	50%	20%
Comments	Forms creamy top layer when serum is left standing	Converted to LDL in plasma	Major transporter of cholesterol in plasma	Major transporter of cholesterol from cells to liver

VLDL = very low density lipoprotein

LDL = low density lipoprotein

HDL = high density lipoprotein

CLASSIFICATION OF LIPOPROTEINS

A. Chylomicrons

Chylomicrons are large particles produced by the intestine, very rich in exogenous triglyceride, poor in free cholesterol and phospholipids and containing about 1 % to 2 % (by weight) protein. Owing to the high lipid : protein ratio, chylomicrons are considered less dense than water and thus float even without centrifugation. Thus, high chylomicron content results in 'milky' plasma ***(Green and Glickman, 1981).***

The apolipoproteins in chylomicrons include apo B - 48, apo A, apo C and apo E. The main function of chylomicrons is to transport exogenous lipid from the intestine to the liver and peripheral cells ***(Green and Glickman, 1981).***

B. Very Low Density Lipoproteins (VLDL)

The liver is an organ of innumerable talents, and the synthesis of fatty acids out of the excess food we eat is one of those talents. Once these fatty acids are made they are put into triglycerides so that they do not take up much space . These endogenous triglycerides are transported in the VLDL form. Phospholipids, cholesterol, apoproteins B - 100, apo C, and apo E are also constituents of VLDL ***(Assmann, 1982).***

There is a wide range of VLDL particle sizes, with a concomitant variation of the chemical compositions. The larger particles are richer in