COMPARISON BETWEEN TWO METHODS FOR MEASURING SERUM LOW DENSITY LIPOPROTEIN CHOLESTEROL

Thesis

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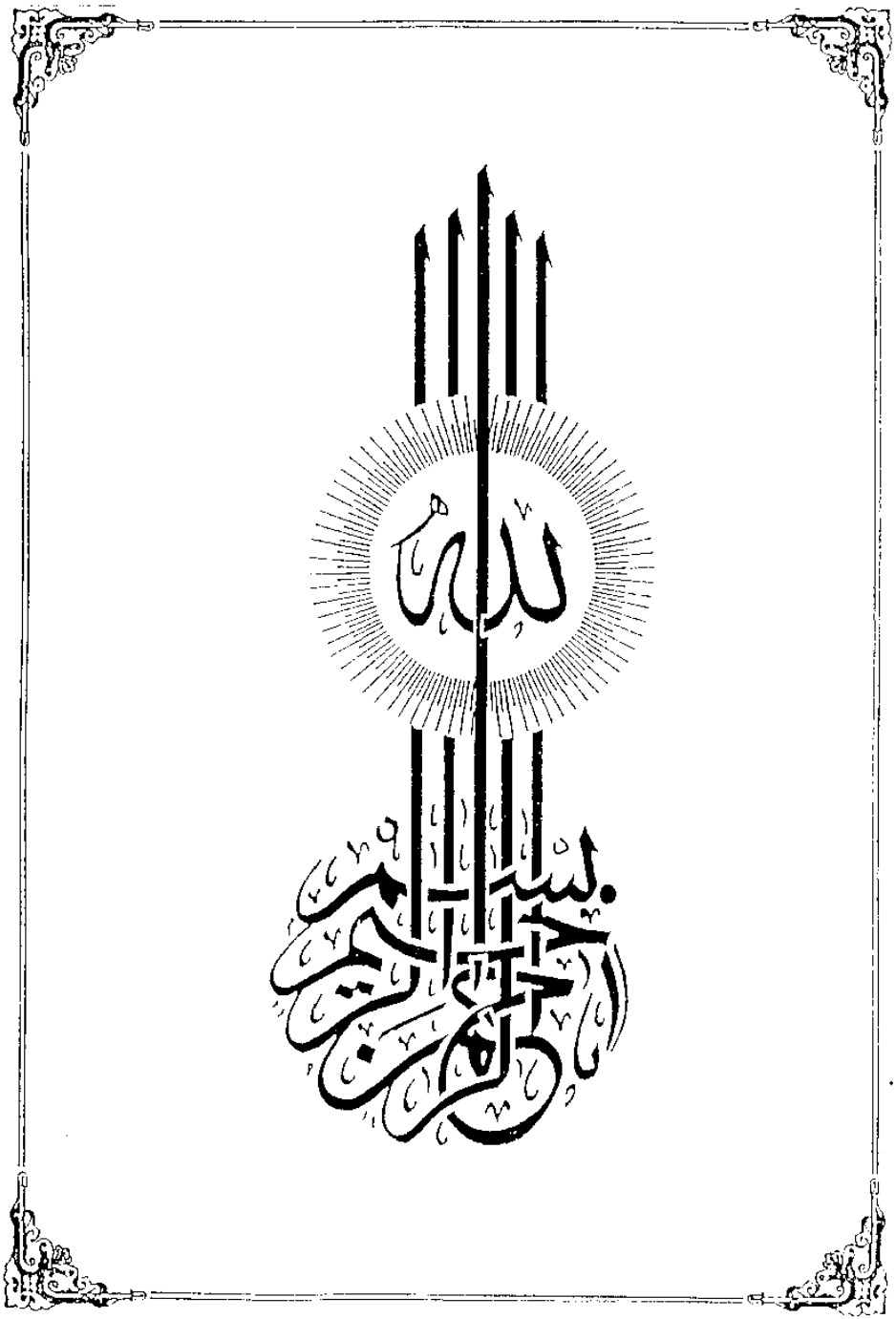

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INTRODUCTION AND AIM OF THE WORK

(I) INTRODUCTION AND AIM OF THE WORK

(A) INTRODUCTION:

Many epidemiological studies revealed a positive correlation between low density lipoprotein (LDL) cholesterol and the incidence of coronary heart disease (CHD) ***(Castelli et al., 1977; Gordon et al., 1977)***. This relationship remained significant after adjustment for the other risk factors in the multivariant statistical analysis ***(Wilson et al., 1980)***. Moreover autopsy studies indicated that LDL and it's specific apolipoprotein B (apo-B) were associated with cholesterol in the atherosclerotic plaques ***(Hoff et al., 1977)***. Also there was a strong positive correlation between the LDL cholesterol levels and the severity of (CHD) as indicated by angiography ***(Miller et al., 1981; Abd El-Fatah et al., 1985)***.

In clinical practice it is advisable to consider high LDL cholesterol values as a positive indicator for coronary atherosclerosis risk and a clue for possible coexistence of other risk factors. Knowing the great clinical value of LDL cholesterol, the development of simple and routine methods for its accurate quantitation is considered an important demand.

Various techniques have been described for the determination of serum LDL cholesterol. The reference

method is the preparative ultracentrifugation, which is very time consuming and laborious for routine purposes. On the other hand, the most commonly used method is the quantitative electrophoresis which is considered expensive and needs special expert. Other practicable methods such as the precipitation methods and the indirect calculation using Friedewald equation have been described but still need evaluation.

(B) AIM OF THE WORK:

The aim of this work is to compare the values of LDL-cholesterol obtained by two different methods. These are the quantitative electrophoresis and the indirect calculation procedure (Friedewald formula), at different triglycerides (TG) levels. A correlation study between LDL cholesterol and apo-B levels in sera will be done.

REVIEW OF LITERATURE

(II) REVIEW OF LITERATURE

(A) LOW DENSITY LIPOPROTEINS

Recent studies showed a striking and independent positive association between low density lipoprotein (LDL) levels and coronary vascular events *(Castelli et al., 1977; Gordon et al., 1977)*. These observations may call for a brief review about structure, function and metabolism of LDL and other components of lipoproteins in order to understand the pathogenesis and molecular mechanism through which LDL may cause or accelerate the vascular disease.

(1) Lipoproteins: (Fig. 1)

Lipoproteins are water soluble complexes of high molecular weight composed of lipids (cholesterol, triglycerides, phospholipids) and one or more specific proteins, called apolipoproteins. Lipoproteins represent the functional unit of transport for water-insoluble lipids in the blood *(Sata et al., 1972)*.

The lipoproteins are divided into various categories according to density as determined by ultracentrifugation *(Havel et al., 1955)*.

a) Chylomicrons:

Chylomicrons are formed in the intestine for the transport of exogenus triglycerides. They are composed of

98-99.5% lipid and 0.5-2% protein. They have density < 0.95 g/ml and float to form a superficial layer on serum when allowed to stand overnight.

b) Very Low Density Lipoproteins (VLDL):

VLDL are formed in the liver and transport the bulk of endogenus triglycerides. They consist of 85%-90% lipid and 10-15% protein. They float at a density < 1.006 g/ml.

c) Intermediate Density Lipoproteins (IDL):

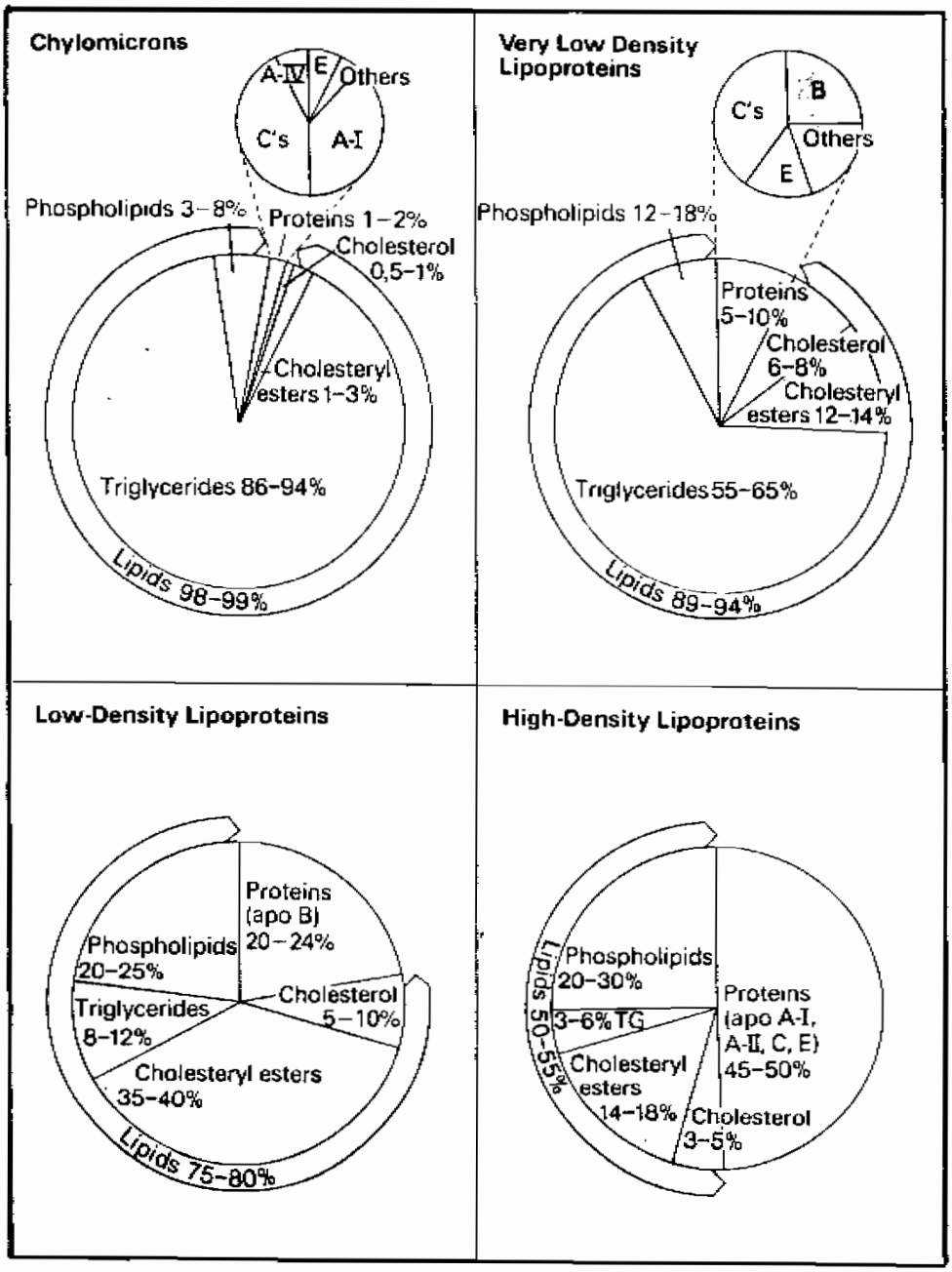
IDL (d = 1.006 - 1.019 g/ml). They are found in the abscence of metabolic disease only in very low concentration and thought to be metabolic products of VLDL or precursor particles of low density lipoproteins.

d) Low Density Lipoproteins (LDL):

Low density lipoproteins (d = 1.019 - 1.063), transport the bulk of cholesterol in the blood. LDL arise as metabolic products of VLDL and contain approximatly 75% lipid and 25% protein.

e) High Density Lipoproteins (HDL):

High density lipoproteins (d = 1.063 - 1.21 g/ml) contain approximately 50% lipid and 50% protein. They are produced by the intestine and liver in a precursor form, then fully developed in plasma. They are capable of picking up cholesterol from cells and carrying it back to the liver.



(FIG. 1) COMPOSITION OF SERUM LIPOPROTEINS (Assman, 1982)

(2) Low Density Lipoproteins:

a) Physical and Chemical Features:

They are heterogenous mixture of macromolecules defined by:

i) Floatation in the preparative ultracentrifuge between densities 1.019 - 1.063 g/ml.

ii) Presence of major protein constituents apolipoprotein-B.

iii) Migration to Beta-position on agarose or cellulose acetate.

iv) By electron microscope LDL molecules appear as spherical particles ranging in size from 200-250 A° *(Jackson et al., 1976)*.

v) By density gradient ultracentrifugation, low density lipoproteins have been further subfractionated into 4 regions: the region of lipoprotein (a), smaller LDL, larger LDL and IDL *(Hoff et al., 1986; Marzetta and Rudel, 1986)*.

b) LDL Composition and Structure:

Low density lipoproteins are water soluble particles of high molecular weight, they are approximately formed of: lipids constitutes 75% of the total LDL mass in the form of