# LIPOPROTEIN (a) AND DIABETIC NEPHROPATHY

Thesis
Submitted in partial fulfillment of the
**Master degree in Endocrinology**

by
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Faculty of Medicine
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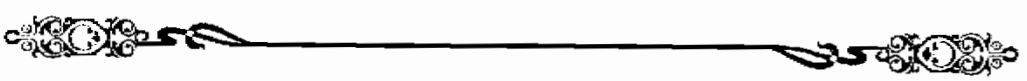
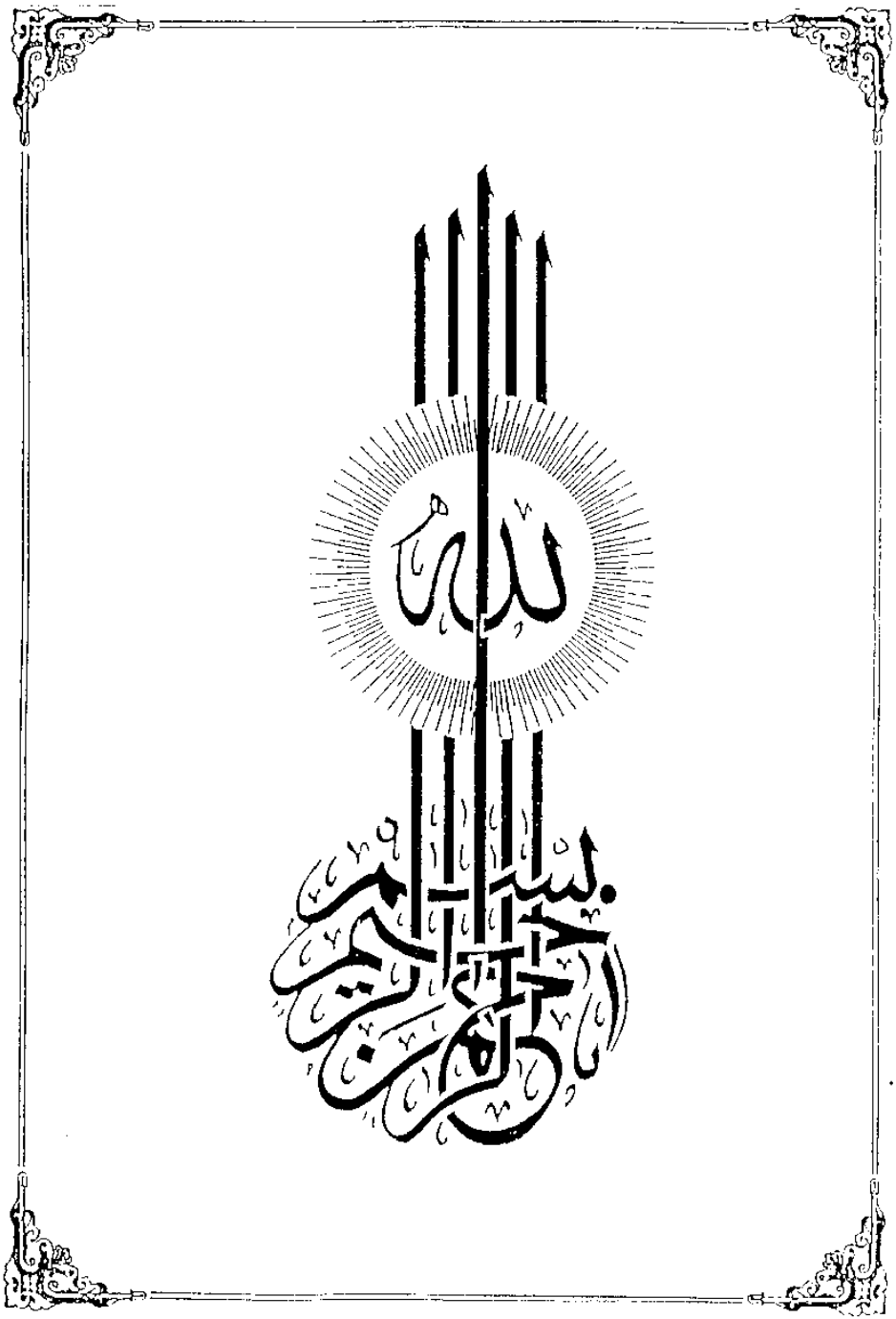
بسم الله الرحمن الرحيم

وفوق كل ذي علم عليم

صدق الله العظيم





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# Introduction and Aim of work

# *Lipoprotein (a) and Diabetic Nephropathy*

## INTRODUCTION :-

Lipoprotein (a), a macromolecular complex found in human serum, is composed of 2 components. One of these is apoprotein (a), which differs from other apolipoproteins and has structural homology with plasminogen of the blood clotting system. The other component is a low density lipoprotein-like particle which contain apo B-100.

Lipoprotein (a) is a quantitative genetic trait which is expressed in a wide range of concentrations within a given population. It exhibits considerable inter- and intra-individual density heterogeneity attributed to apo (a) isoforms.

Recently, clinical interest has been paid to the disturbances of lipoprotein (a) concentrations in relation to cardiovascular disease. High concentrations of lipoprotein (a) were reportedly associated with increased risk of coronary artery disease and cerebral infarction.

## AIM OF THE WORK :-

The aim of the work is to;

- Find out the behaviour of lipoprotein (a) in various renal conditions in type II diabetics in the following groups

  Group I; non proteinuric diabetics

  Group II; diabetics with microalbuminuria

  Group III; diabetics with macroalbuminuria

- Study the relationship between the above diabetic states and normal non diabetic controls with respect to lipoprotein (a)

- Find out the level of lipoprotein (a) in controlled diabetics in comparison with uncontrolled diabetics.

# Review of Literature

# *Lipoproteins and Apoproteins*

## LIPOPROTEINS :-

Lipids are insoluble in aqueous media, including that of plasma. It is only when the hydrophilic lipids are bound to protein (lipid-protein complexes called "lipoproteins") that they become soluble in the blood stream *(Osborne and Brewer, 1977).*

A lipoprotein can be described as a globular structure with an outer solubilizing coat of protein, phospholipid, and free cholesterol and an inner hydrophobic, neutral and core of triglycerides and cholesterol esters *(Scanu and Landsberger, 1980).*

In clinical medicine, lipoproteins in plasma are typically classified on the basis of their electrophoretic mobility and hydrated density *(Tatami et al., 1981)* into chylomicrons (CM), very low density lipoproteins (VLDL), intermediate density lipoproteins (IDL), low density lipoproteins (LDL), high density lipoproteins (HDL), and lipoprotein (a) (Lp {a}). (Diagram 1) *(Koplan and pesce, 1989).*

| Lipoprotein | Density (gm/ml) | Size |
|---|---|---|
| CM | < 0.96 | > 300 |
| VLDL | 0.96 - 1.006 | 300 - 800 |
| IDL | 1.006 - 1.019 | ~ 245 |
| LDL | 1.03 - 1.063 | 200 - 225 |
| Lp (a) | 1.05 - 1.08 | 236 - 255 |
| HDL | 1.063 - 1.21 | 75 - 100 |

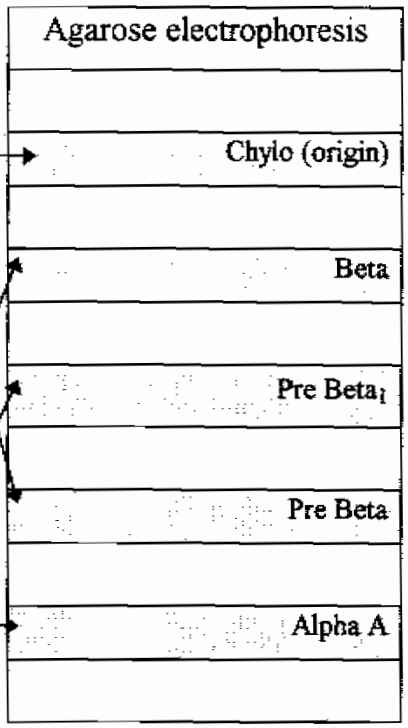


**Diagram (1);**

**Classification of the major types of lipoproteins according to some basic physical properties and agarose gel electrophoresis** *(Koplan and Pesce, 1989).*

Chylo = Chylomicron,

Beta = Beta lipoprotein,

Pre $Beta_1$ = Prebeta-1 lipoprotein,

Pre Beta = Prebeta-2 lipoprotein,

Alpha A = Alpha lipoprotein

The composition of lipoproteins can be summarized as follows with respect to triglycerides, cholesterol, phospholipid, and protein (apoprotein) contents (table 1) *(Shaefer and Levy, 1985).*

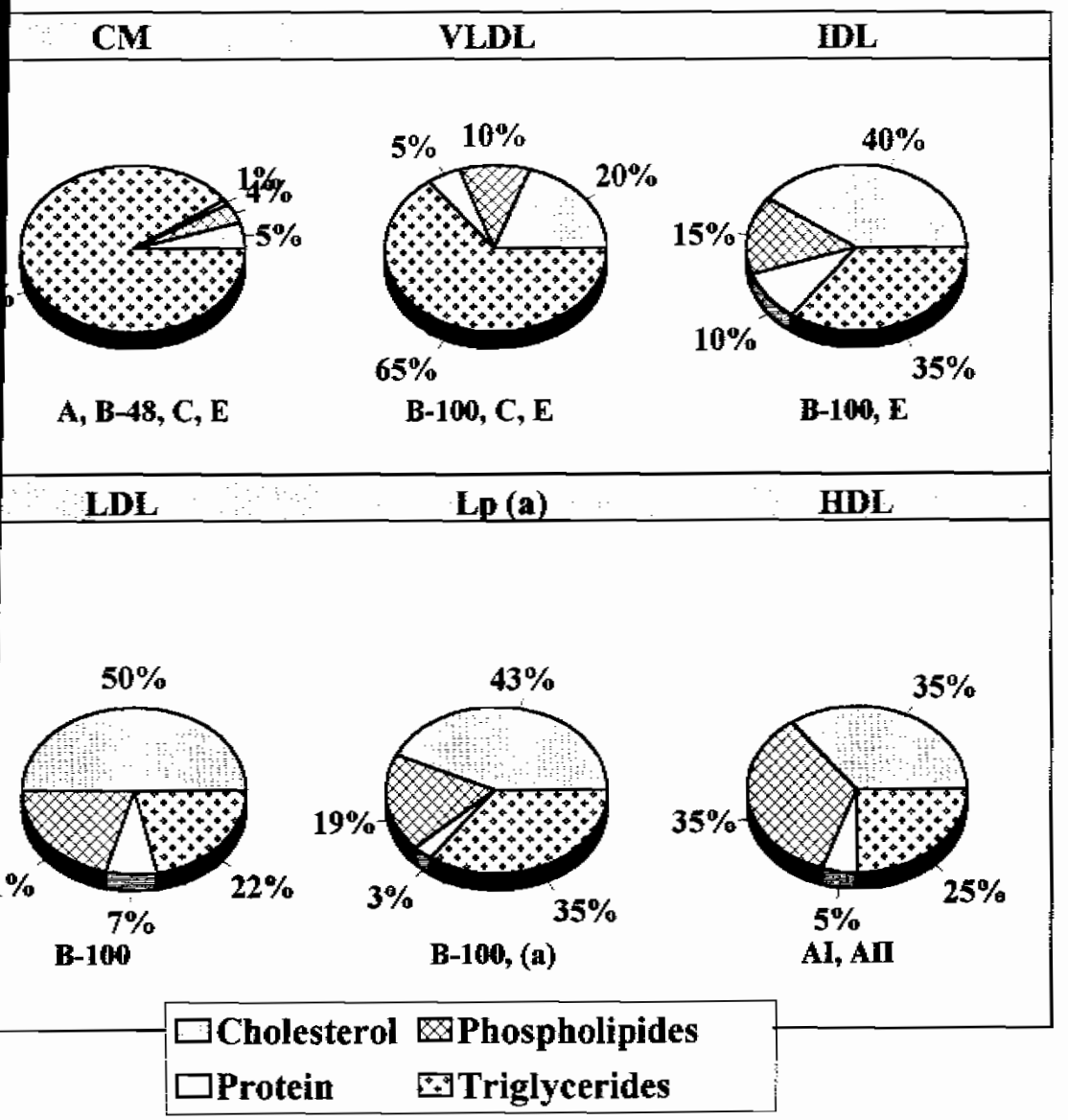


**Table (1);**

**Composition of lipoproteins with the major apoprotein classes present in each** *(Shaefer and Levy, 1985).*

The main functions of these lipoproteins may be collectively expressed in the following table (Table 2) *(Rifai, 1986).*

| Lipoprotein | Function |
|---|---|
| CM | Transport of exogenous triglycerides |
| VLDL | Transport of endogenous triglycerides |
| LDL | Transport of cholesterol from liver to other tissues |
| Lp (a) | Functional significance undetermined<br>Proven to be atherogenic |
| HDL | Transport of cholesterol from peripheral tissues to liver |

**Table (2);**

**Principal functions of the lipoproteins**

*(Rifai, 1986).*

## APOLIPOPROTEINS :-

The protein components of plasma lipoproteins termed apo-lipoproteins or apoproteins appear to be synthesized only in two sites. The liver and the mucosal cells of the small intestine *(Brewer et al., 1988).*

There are many apoproteins in human plasma being identified as apo A-I, apo A-II, apo A-IV, apo B-48, apo B-100, apo C-I, apo C-II, apo C-III, apo D, apo E-2, apo E-3, apo E-4, apo E-5, apo F, apo G, apo, H, and apo (a) *(Marshall, 1990).*

The different apoproteins of human plasma lipoproteins can be summarized in Table (3) *(Harper, 1993).*

## Importance of apoproteins :-

- The help to solubilize cholesterol and triglycerides by interacting with the other major classes of lipids found in lipoproteins namely phospholipid.
- They regulate the reaction of these lipids with enzymes such as LCAT (lecithin cholesterol acyle transferas) and lipoprotein lipase.
- They bind to cell surface receptors and thus, determine the site of the uptake and rate of degradation of other lipoprotein constituents, notably cholesterol *(Thompson, 1984).*

| Apo-protein | Lipoprotein | Molecular mass (Da) | Additional remarks |
|---|---|---|---|
| A-I | HDL, chylomicrons | 28,000 | Activator of lecithin, cholesterol acyl transferase (LCAT).<br>Ligand for HDL receptor |
| A-II | HDL, chylomicrons | 17,000 | Structure in 2 identical monomers joined by a disulfide bridge<br>Inhibitor of LACT ? |
| A-IV | Secreted with chylomicrons but transferes to HDL | 46,000 | Associated with the formation of triacylglycerol-rich proteins<br>Function unknown |
| B-100 | LDL, VLDL, IDL | 550,000 | Synthesized in the liver<br>Ligand for LDL receptor |
| B-48 | Chylomicrons<br>Chylomicrons remnants | 260,000 | Synthesized in intestine |
| C-I | VLDL, HDL, Chylomicrons | 7,600 | Possible activator of LCAT |
| C-II | VLDL, HDL, chylomicrons | 8,916 | Activator of extrahepatic lipoprotein lipase |
| C-III | VLDL, HDL, chylomicrons | 8,750 | Several polymorphic forms depending on content of sialic acid |
| D | Subfraction of HDL | 20,000 | Function unknown |
| E | VLDL, HDL, chylomicrons, chylomicrons remnants | 34,000 | Present in excess in the B-VLDL of patients with type III hyperlipoproteinemia.<br>The sole apoprotein found in HDL-C of diet induced hypercholesterolemic animals<br>Ligand for chylomicron remnant receptor in liver and LDL receptor |
| Apo (a) | LP (a) | 280,000 | Role in atherosclerosis |

**Table (3);**

**Apoprotein of human plasma lipoprotein** *(Harper, 1993)*