LIPOPROTEIN AND FREE FATTY ACIDS IN CONTROLLED DIABETIC PATIENTS

THESIS

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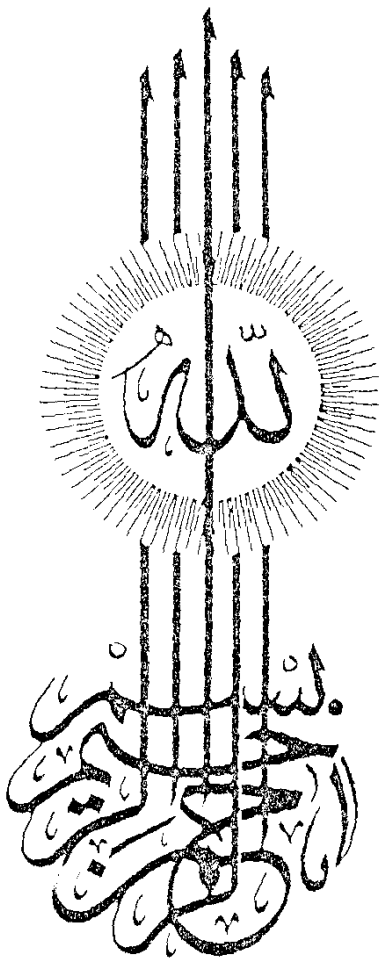

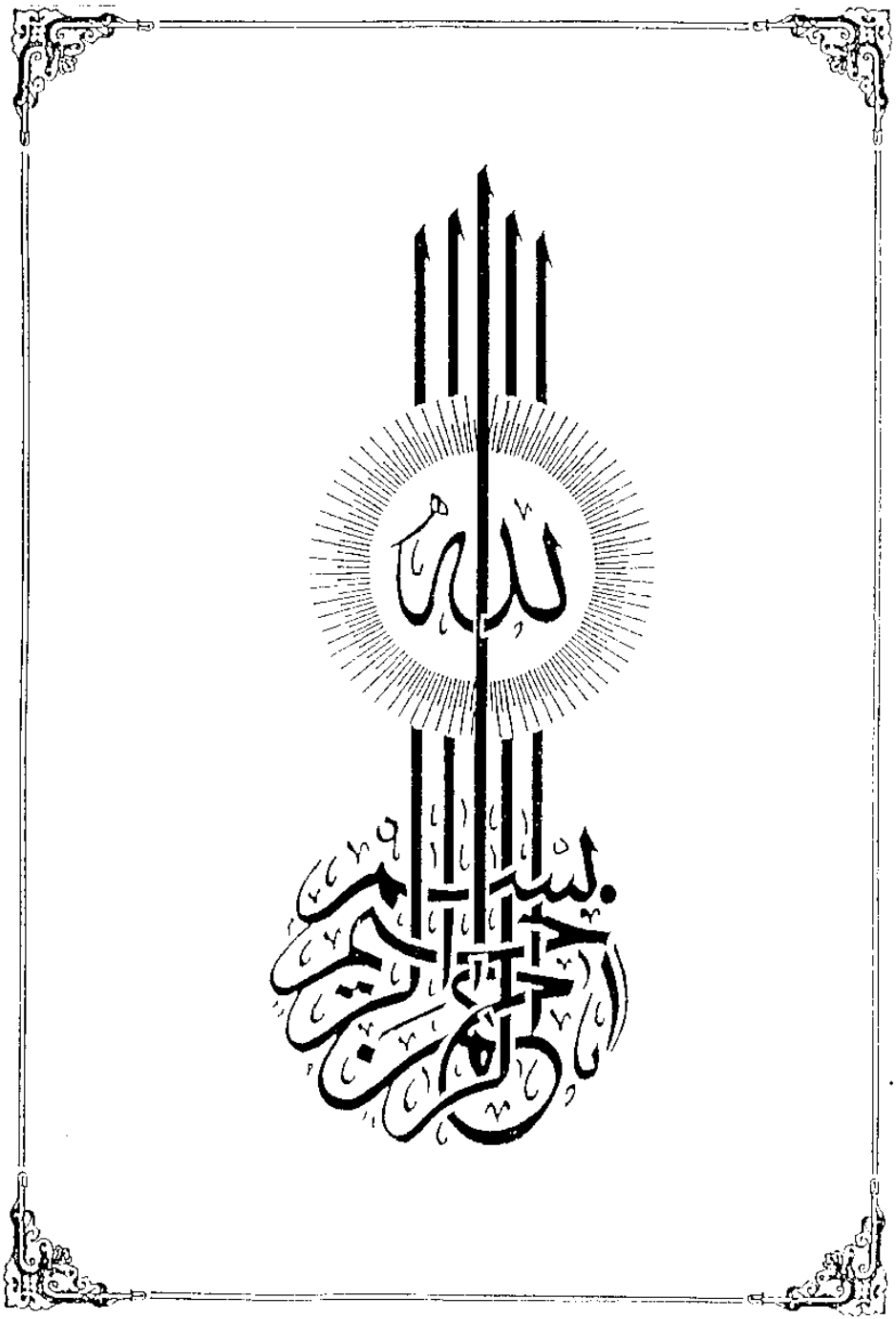

" TO MY WIFE AND MY SON "

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C O N T E N T S

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AIM OF WORK

Atherosclerosis in the diabetic population tends to occur at an earlier age and with greater severity than in the non diabetic population. Hyper lipidemia and lipoprotein abnormalities play the major role in atherogenesis. In diabetes mellitus many authors report abnormalities of the lipid pattern.

Our aim is to study the lipoprotein pattern and free fatty acids in diabetic patients controlled either with insulin or oral sulfonylureas, and compare these groups with healthy control.

This is to clarify the most efficient means of treating glucose intolerance and normalizing lipid dearangement to prevent atherosclerotic complications in diabetics.

REVIEW OF LITERATURE

INTRODUCTION

The relationship between diabetes mellitus and lipoproteins is of considerable interest, patients with diabetes have greater incidence of coronary artery disease than non diabetic population of similar age (Joseph & Gustav, 1979). There are certain risk factors, such as hypertension, cigarette smoking, and hyper lipidemia, that appear to play a role in the pathogenesis of atherosclerosis, these same factors are operative in diabetes (Kirk et al., 1980).

The major causes of morbidity and mortality in patients with diabetes mellitus are related to diseases of microcirculation and macrocirculation. Microcirculatory changes are most commonly found in the capillaries of the eyes, the kidney and in other areas of the body. The disease of the large sized and medium sized arteries is atherosclerosis, which appears to be indistinguishable from that observed in non diabetic patients (Strandness et. al., 1964). However the disease appears at an earlier age in diabetic, is more extensive, and is associated with a higher morbidity and mortality (Santen et. al., 1972).

Of the total lipids in human, blood total cholesterol forms about 33 percent and the phospholipids about 35 %, the remainder is neutral fat. In normal Egyptians the mean total lipids have been found to be 412.2 mg % ± 10.9 (Raafat, 1973).

Regarding the lipid and lipo-protein fractions in normal Egyptians, the mean total plasma cholesterol was 175.3 mg % and the lipoprotein pattern was alpha fraction 120.1 mg %, beta fraction 212.5 mg % and the non mobile fraction 86.5 mg %. The beta/alpha lipoprotein ratio was 1.8.

In Diabetic Egyptians, there was marked derrangement of the lipids and lipoprotein pattern.

The total serum lipids have been found to be 472.1 mg % and total plasma cholesterol 218.6 mg %. Of the lipoprotein fractions, alpha forms 93.1 mg %, beta 275.9 mg % and non mobile fraction 102.9 mg %. The beta/alpha ratio amount to 3.25 (Raafat, 1973).

DIABETES MELLITUS

Definition of Diabetes

Diabetes mellitus is not a disease in the classic sense. It has no distinct and definable pathogenesis, aetiology, invariable set of clinical findings, specific laboratory tests, or definition and curative therapy. Rather, it should be viewed as a syndrome of clinical entity which can involve any or all of long symptoms and clinical laboratory findings which show a variable response to therapy (Porte and Halter, 1981).

Inspite of its complexity, diabetes mellitus may be defined as a disorder of metabolism of which the most obvious component is a diminished ability to utilize carbohydrate, manifesting itself as hyperglycaemia, glucosuria, tendency to ketosis and typical complications (Ghalioungui and Ghareeb, 1978).

According to Porte and Halter (1974), diabetes mellitus has five main components consisting of :

(1) Biochemical changes, especially with regard to the carbohydrate, lipid, protein and nucleotid metabolism.

(2) Microscopic and macroscopic alteration in various organs of the body consisting especially of a characteristic microanigiopathy, precocious atherosclerosis and pancreatic islet disorder.

(3) Deficient insulin action.

(4) Increased glucagon action.

(5) Clinical manifestations due to altered hydration and osmolarity, micro-angiopathies and atherosclerosis.

It is a complex chronic metabolic disorder characterized in most cases by relative or absolute insulin insufficiency in which an inherited susceptibility plays an important part (Felig, 1971 and Oakley, et al., 1973).

Diabetes mellitus is not a disease entity, but multiple diseases affecting different organs with one common basic pathology, vis: laying down of PAS positive material in the basement membranes leading to their thickening or which is commonly called microangiopathies. It is characterized by hyperglycemia and glycosuria, based on a disturbance in carbohydrate, fat, protein and mineral metabolism and mainly due to lack of

effective available insulin (Ghareeb, 1972).

Typical vascular and neuropathic manifestations of diabetes may occur in patients with genetic predisposition to diabetes with mild carbohydrate intolerance and normal fasting blood glucose levels (Fajans, 1971).

Furthermore there are tremendous differences among diabetic patients with respect to the extent of development of the various disorders, the time and the presentation of their manifestations.

Diabetes mellitus may be associated with atherosclerotic or microangiopathic vascular changes and neuropathy, but hyperglycemia may be manifested years before these vascular changes or neuropathy are recognized clinically, and the reverse may occur (Elenberg, 1963).

Recent Classification of Diabetes Mellitus :

When diabetes is inherited, it is called essential or idiopathic, while secondary diabetes is related to some other diseases or percipitated by drugs. Some patients with secondary diabetes have a hereditary predisposition to develop diabetes, i.e. are prediabetics. Herditary idiopathic diabetes is classified into insulin dependent diabetes mellitus (IDDM) and non insulin dependent diabetes mellitus (NIDDM), (Porte and Halter, 1981).

Table (I): Classification of Diabetes Mellitus, according to Williams (1981).

Traditional Clinical Classification (with Alternate Nomenclature)	NID Diabetes Data Group Classification
(1) Juvenile Onset Type Diabetes(JOD) a) Ketosis-prone diabetes b) Juvenile-onset diabetes c) Severe diabetes d) Brittle diabetes	(1) Insulin Dependent Diabetes Mellitus, Type I (IDDM)
(2) Maturity-onset-Type Diabetes(MOD) a) Ketosis resistant diabetes b) Adult onset diabetes (AOD) c) Mild diabetes d) Stable diabetes e) Obesity-hyperglycemia f) Maturity onset diabetes	(2) Non-Insulin-Dependent Diabetes Mellitus, type II, (NIDDM): 1- Nonobese NIDDM 2- Obese NIDDM
(3) Maturity onset Type Diabetes in the young (MODY) a) Familial maturity diabetes b) Maturity onset diabetes of youth	
(4) Gestational Diabetes	(4) Gestational Diabetes
(5) Secondary Diabetes	(5) Diabetes Mellitus and Impaired Glucose Tolerance associated with other conditions
(6) Congenital Insulin Resistance with Acanthosis Nigricans	(6) Diabetes Mellitus Secondary to congenital Insulin Receptor Deficiency

P.T.O.