Assessment of Hepatic function through estimation of Serum Glycoproteins In Egyptian Diabetics

T H E S I S

Submitted in Partial Fullfilment for
M.S. degree of "General Medicine"

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1986

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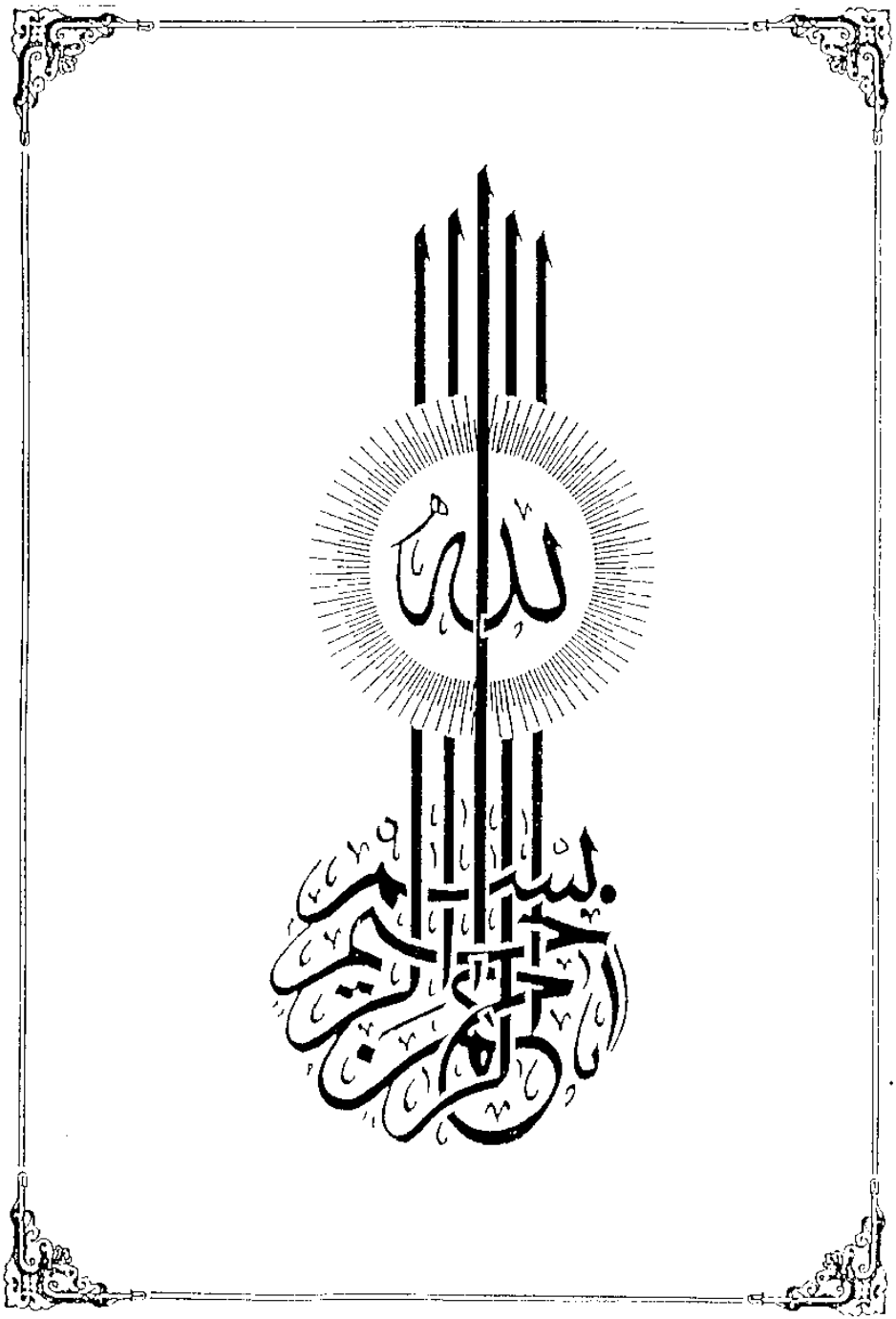

ACKNOWLEDGEMENT

I would like to express my gratefulness to my professor Dr. Mohamed Awadallah Salam, professor of Internal Medicine Ein Shams University, for his meticulous supervision, valuable knowledge helpful directions, countinous support, offered facilities and great interest which were much valuable for the production of this work.

I am deeply express my gratefulness to my professor Dr. Yehia Mahran, head professor of Internal Medicine Ein Shams University.

I would like to express my deepest gratitude to assistant professor Dr. Laila Abou El Magd, assitant professor at Clinical Pathology, Ein Shams University, for her kind cooperation, continous support and valuable help during this work.

I wish to thank Dr. Mohamed Ahmed Ghareb for his kind attitude and fine art which were of great help.

I am much thankful to Dr. Mohsen Maher whose kind help, advice and lot of effort helped greatly in the production of this work.

INTRODUCTION AND AIM OF WORK

In view of the fact that the liver is the principle organ concerned with the metabolism of carbohydrates, lipids and proteins. It is not suprising to find that diabetes mellitus is commonly associated with one form or another of hepatic affection (Sherlock, 1981).

Hepatic changes have been reported by various groups of workers both in experimental animals and in man (Sulinovici and Roginski, 1980, Sherlock, 1981). Thus an enlarged liver with firm roundded non-tender border has been found frequently in subjects suffering from non-insulin dependent diabetes mellitus (Cardell, 1980).

Similarly, a greatly enlarged, firm and tender liver has been observed in insulin dependent diabetes particularly in uncontrolled cases as well as in patients presenting with diabetic keto acidosis (Godman, 1953).

Routine liver function tests are usually normal in well controlled diabetics; however higher than normal alkaline phosphatase levels have been reported in diabetic patients

(Camerini, Davalos et al, 1962). Also hypertriglyceridaemia has been reported (Awadein, 1984).

Glycoprotein bio synthesis is of particular interest in diabetes, since it would seem reasonable that significant alterations in glucose metabolism could be reflected in the synthesis of the carbohydrate-containing protein. Changes in the palsma levels of glycoproteins has been reported by Jonsson and Wales (1976).

This work was performed to study the changes in serum glycoproteins (prealbumin, haptoglobin and d2 macroglobulin) In Egyptian diabetics, for detection of hepatic involvement and to see if these changes are more sensitive than standard liver function tests.

DIABETES MELLITUS

DEFINITION, CLASSIFICATIONS

AND AETIOLOGY

Diabetes mellitus is not a disease in the classic sence since it has no distinct or definable pathogenesis, aetiology, set of clinical findings, specific laboratory tests or definitive and curative therapy. It should be rather viewed as a syndrome or clinical entity which can involve any or all of a long list of symptoms as well as clinical and laboratory findings and thus showing variable responce to therapy. the term diabetes mellitus, then is one of converience for the physician, rather than one that conveys definite pathologic meaning for the patient (Williams, 1981).

In making a clinical diagnosis of diabetes mellitus, four aspects of the picture should be considered :

1) Hyperglycaemia : there is an abnormality of carbohydrate metabolism resulting in hyperglycaemia and often associated with accelerated fat and protien catabolism. This abnormality probably conributes to other features but seems unlikely to be their sole cause.

2) Large vessel disease : in the form of accelerated atherosclerosis and medial calssification.

3) Micro-vascular disease : Characterized by thickening and abnormal function of capillary basement membrane. These capillary-related lesions are often termed micro-vascular or small vessel concomitants of diabetes.

4) Neuropathy : revealing itself as peripheral sensory and motor defects as well as autonomic nervous system dysfunction, segmental demylination and abnormalities of Schwann cells.

Since, non of these finings is specific for diabetes, as each can be foud in other diseases. The final decision in diagnosing diabetes mellitus should be based on both clinical and laboratory grounds.

Classification of diabetes mellitus :

At the beginning, diabetes mellitus was classified on the basis of the age of onset of the diabetic state into juvenile onset and maturity onset varieties. Lately, it has been proved that these terms are unsatisfactory since some patients develop diabetes in adult life and still can suffer insulin dependent diabetes, whereas the maturity onset variety can also present in the young. In addition, it has become clear that not only there is an age difference but

there are also genetic factor (S) differentiating between the various clinical types.

In 1975, Tattersal and Fajans reported a rare type of diabatic pressentation, which is the maturity onset diabetes of youth. Patients with this presentation usually have mild symptoms, and ketonuria as well as hyperglycaemia that can be controlled without insulin therapy. A strong family history of diabetes usually exists. An autosomal dominent made of transmission seems most likely on the basis of family studies. The micro and macro-vascular complications seem to be rare.

Cudworth and Woodrow (1976), pointed out that insulin-dependent diabetes diagnosed before or after the age of 30 have genetic similarity at least in respect of an increased frequency of the HLA allelel. In 1976, Cudworth proposed the term of type I to describe all patients with insulin-dependent diabetes mellitus, regardless of the age of onset. In this connection, Bottazzo and Doniach (1976) reported the presence of circulating islet cell antibodies in all patients classified as insulin-dependent diabetes mellitus. These workers subdivided Cudworth type I patients into type IA and type IB. In the former group, the antibodies are transient and not detectable before the onset of diabetes,

where as in type IB the antibodies may be detected before the onset and may persist in the circulation afterwards, together with the presence of other autoimmune antibodies to other endocrine tissues.

Regarding type II diabetes mellitus, Cudworth (1976), included all patients previously known as maturity-onset diabetes mellitus in this entity.

In 1979, an international workgroup sponsored by the National Diabetes Association, developed a classification of diabetes and other categories of glucose intolerance, based on contemporary knowledge of this heterogenous syndrome. This classification was accepted by the World Health Organization. It is proposed to be used as a uniform in which to conduct clinical, epidemiologic research and to avoid the factors of age.

The salient features proposed in the classification are :

(1) The insulin-dependent, ketosis-prone type of diabetes, which is associated with increased frequency of certain histocomptability antigens

(HLA) on chromosome 6 and with islet cell antibodies is called Insulin-dependent diabetes mellitus (IDDM). This type of diabetes is the one which was inappropriately termed juvenile diabetes and since, it can occur at any age, it is recommended that diagonsis based on age of onset be eliminated.

(2) The non insulin-dependent, non ketosis prone type of diabetes, which is not secondry to other diseases or conditions is designated non-insulin dependent diabetes mellitus (NIDDM). This subclass has been further subdivided on the basis of the presence or absence of obesity into obese NIDDM and non-obese NIDDM, respectively. Patients in this subclass can be further characterized by the type of treatment they receive whether insulin, oral hypoglycaemic agents or diet.

(3) The types of diabetes caused by other conditions found in increased frequency with other diseases implying an aetiologic relationship are considered a third subclass of diabetes mellitus (diabetes associated with certain conditions and syndromes). This subclass has beer further subdivi-

ded according to the known or suspected aetiologic relationships.

(4) The class of gestational diabetes which is restricted to women in whom glucose intolerance develops or is discovered during pregrancy.

(5) Inividuals with plasma glucose levels intermediate between those considered normal and those considered diabetic should be termed impaired glucose tolerance. Terms such as chemical, latent, borderline, subclinical and asymptomatic diabetes which have been applied to persons in this class should be abandoned, since use of the term diabetes invokes social, psychologic, and economic sanctions that are justified in light of the lack of severity of their glucose intolerance.

(6) Individuals with normal glucose tolerance who have experienced transient hyperglycaemia either spontaneously or in respence to indentifiable stimuli are classed as previous abnormality of glucose tolerance, and that terms of latent diabetes and prediabetes be abandoned, since these incividuals

are not diabetic.

(7) Individuals who are at substantially higher risk than the general population to develop diabetes are considered to have potential abnormality of glucose tolerance, and that the terms potential diabetes and prediabetes be abandoned, since these individuals are not diabetics.

Aetiology and Pathogenesis of Diabetes Mellitus :

Searching for the possible aetiologic factors involved in the development of diabetes, certain epidemiologic, genetic, immunologic aspects which throw new light onto the natural history of the condition and possible interaction of HLA-Linked genetic susceptibility and virus infection.

Cudworth et al (1977), observed that age incidence in the childhood diabetics was bimodal with a peak age of onset at about 11 years and another at the early twenties. They suggested genetic and/or environmental influences to be operating at these different ages. A further support for this assumption is the seasonal peaks observed in autumn and winter favouring the involvement of environmental factors initiating or precipitating the disease (Bloom et al, 1975).

Concerning the role of nutrition as one of the environmental factors in genesis of the diabetic syndrome, two major hypothesis have been formulated linking diet with diabetes mellitus. These include the fat hypothesis of which Himsworth (1935) was the protagonist and the sugar hypothesis championed by Cohen et al (1961) and Yudkin (1964); each claiming that high intake of a particular nutrient increases the risk of diabetes. Two other nutritional factors namely, trivalent chromium deficiency (Hambidge, 1974) and dietry fibre depletion (Trowell, 1975) have been considered to have an aetiologic role in diabetes.

In contrast, Kahn et al (1971) as well as West (1972) found on evidence for glucose intolerance to be directly associated with higher levels of fat, carbohydrate or sucrose consumption. Similar negative conclusions regarding the role of total energy intake and sucrose intake in diabates were arrived at by Keen and his collegues (1979).

Obesity is a common association with maturity onset diabetes. However the mechanism as well as its relationship to specific diatery factors are not totally agreed upon. This is partly due to the lack of correlation between the degree of obesity and hyperglycaemia which may be due to