STUDY OF ENDOCRINE PANCREATIC FUNCTIONS AND LIVER FUNCTIONS IN DIFFERENT TYPES OF DIABETIC PATIENTS BEFORE AND AFTER TREATMENT

رسالة

THESIS

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(B.Sc. 0f Biochemistry)

In Partial Fulfilment

For the Degree of

M.Sc. In

BIOCHEMISTRY

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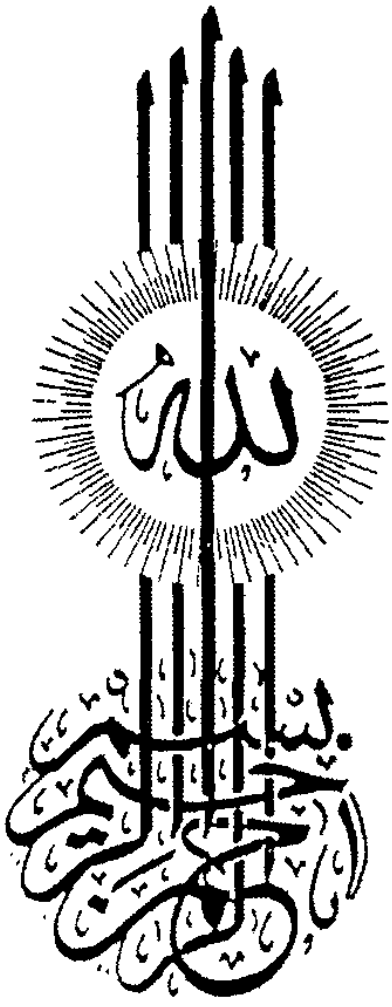
1993



" وعلمك ما لم تكن تعلم
وكان فضل الله عليك عظيما "

صدق الله العظيم

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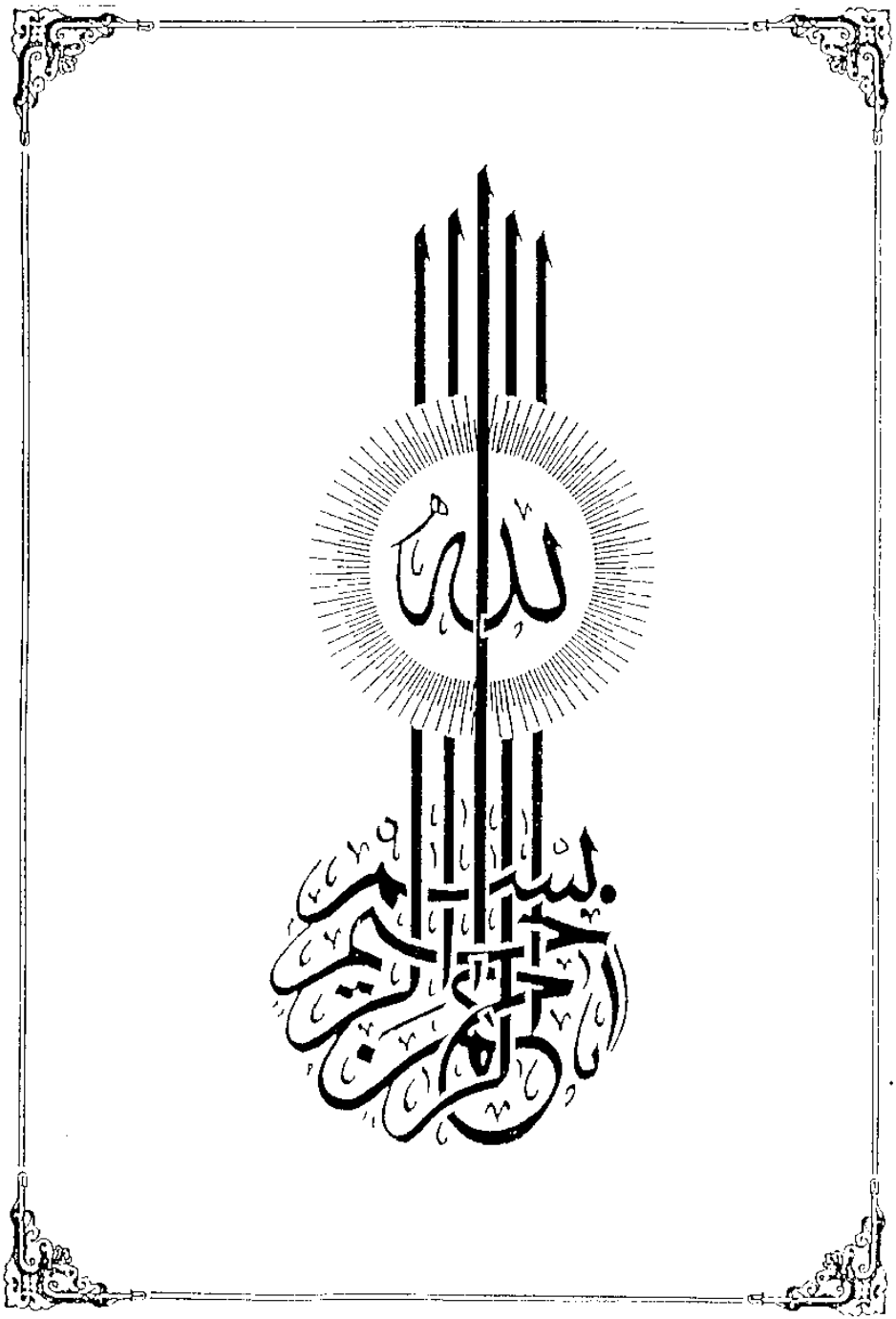

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ACKNOWLEDGEMENT

I offer my deepest gratitude to ***Prof.Dr. ZEINAB ZAKI EL DARDIRI ,*** Professor of Biochemistry, Faculty of Science, Ain Shams University, for soothing the work, valuable assistance and continuous encouragement throughout this thesis. Really, no words can satisfy and explain may gratitude and thanks for her kind help

I am greatly indebted to ***Dr. SAMIR MOHAMED ATTIA,*** Cheif of Chemical Pathology, Military Medical Acadmy, for giving every possible help,advice and efforts in supervising this thesis as well as providing laboratory facilities .

I am also very grateful to ***Dr. NADIA YOUSSEF SADEK MORCOS,*** Lecturer of Biochemistry, Faculty of Science, Ain Shams University, for her valuable assistance and sincere guidance which she offered throughout this work as well as for reading and criticizing the manuscript.

Last but not least, I would like to express my gratitude to all patients, who participated willingly and kindly in this work, wishing them all the best of health, and hoping that this work may be of some value to them .

I hope that my modest work will be up to the level of their satisfaction.

Thanks for every body who made this work possible .

Before all and above all, thanks to my God .

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AIM OF WORK

AIM OF WORK

Diabetes mellitus affects the functions of a good number of endocrine glands. Many studies were made to illustrate the interrelationship between diabetes mellitus and these organs. From their study of C-peptide levels in different types of diabetic patients found that, C-peptide levels help consideraly in the selection of treatment and its measurment reflects pancreatic beta cell function in additor to that of insulin.

This syndrom is associated with an increased risk of certain associated disease, including those involving the liver. The liver has a major role in glucose hemeostasis.

This work is designed to study the endocrine pancreatic functions and liver functions in different types of diabetic patients before and after treatment.

Introduction

HISTORICAL ASPECT OF DIABETES

In accounts of the history of diabetes, it is stated that in the Egyption Papyrus Ebers (about 1500 B.C.), there was mention of polyuria and that"honey urine" was noted by Sushrutha in India in 400 B.C. The first good clinical description of the disease was made by Celsus and the name "Diabetes" was introduced by Aretaeus, a Roman physician but it was not until two centuries later that another Greek physician, gave the name diabetes (a siphon) .

Avicenna (Ibn-Sina) (980 - 1087) , gave a remarkably good description of diabetes, including some of its complications such as gangrene .

However, although it had been known for centuries that diabetic urine tasted sweet, it remained for Willis in 1674 to add the observation "as if imbued with honey and sugar". The name diabetes mellitus (mellitus=honey) was thus established . A century after Willis, Dobson demonstrated that the sweetness was, indeed, due to sugar and that urine was subject to alcoholic and acetic fermentation .

Furthermore Cawley in 1788, discussed the role of the pancreas in the pathology of diabetes .

Trommer (1841), and Fehling (1848), developed the well known cupric oxide tests for urinary sugar .

Langerhans found accumulations of special cells in the pancreas (1869), which were later named "Langerhans' islets".

In (1889), a great Landmark was reached when Mering and Minkowski produced diabetes in dogs by total pancreatectomy .

A series of papers published around 1900 by Szobolev gave the clearest explanation of the function of the islets .

The greater step forward came in (1922), when Banting and Best, a canadian physiologist and a biochemist, succeeded in extracting a substance

from the pancreas with hypoglycemic properties "Insulin" and treated the first human diabetic by this substance .

The first crystalline insulin was then prepared and its molecular weight was determined by Svedberg ,(1931), using the ultra centrifuge technique .

The introduction of the oral hypoglycemic agents by Loubatieres (1957), provided another stimulus because studies designed to elucidate the mode of action of these drugs led investigators into a closer examination of the pathophysiology of diabetes and the mode of action of insulin

In (1968) Steiner et al., discovered the existence of proinsulin, a single chain precursor of insulin .

DEFINITION AND CLASSIFICATION OF DIABETES MELLITUS

Diabetes Mellitus is not a disease in the classical sense but is more probably a syndrom . It may be defined as a metabolic disorder of which hyperglycemia (with or without glucosuria) is the essential feature.

In (1979) , The National Diabetes Development Group developed together with the main associations for the study of diabetes, the classification divided diabetes according to insulin dependence .

1 - Type I, insulin dependent diabetes mellitus (IDDM) :

The first subclass of diabetes is usually characterized clinically by abrupt onset of symptoms, insulinopenia, and dependence on injected insulin to sustain life, and proneness to ketosis. Classically, this type of disease occurs in juveniles, and it was formerly termed juvenile diabetes, ketosis-prone diabetes.

Genetic determinants are thought to be important in most patients, as expressed by the assocaited increased or decreased frequency of certain histocompatibility leucocyte antigens (HLA) on chromosome 6 (Cudworth and Woodrow, 1976).

Abnormal immune responses and autoimmunity are thought to play an etiologic role, and islet cell antibodies are frequently present at diagnosis in this type of diabetes (Irvine, 1977).

II - Type II , non- insulin dependent diabetes mellitus (NIDDM):

The second subclass of diabetes, frequently presents with minimal or no symptoms referable to the metabolic aberrations of diabetes. Patients with NIDDM are not dependent on insulin for prevention of ketonuria and are not prone to ketosis.

However, they may require insulin for correction of symptomatic, or persistent, fasting hyperglycemia if this cannot be achieved with the use of diet or orel agents.

Such patients may develop ketosis under special circumstances, such as severe stress precipitated by infections or trauma.

There may be normal levels of insulin, mild insulinopenia, or above normal levels of insulin associated with insulin resistance (Turner and Holman,1976). The whole range of insulin responses to glucose from low to supranormal has been found in patients of this subclass.

NIDDM is also heterogeneous in nature. Although in most patients who develop NIDDM the onset is after age 40,the NIDDM type also occurs in young persons MODY (Maturity Onset Diabetes of Young) who do not require insulin and are not ketotic. Consequently , age at onset is again not recommended as a criterion by which to classify an individual, and the terms adult or maturity onset, ketosis resistant diabetes, should be abandoned as classifying terms (Fajan,1977).

NIDDM also has a genetic basis, which appears to be stronger than in IDDM, as evidenced by a more frequent familial pattern of occurrence.

Environmental factors superimposed on genetic susceptibility are undoubtedly involved in onset of the NIDDM types. Although small changes in weight may be important, NIDDM has been subdivided according to the absence or presence of obesity, as 60-90 % of all NIDDM patients are obese. In persons with this type of diabetes, characteristic aggregation of HLA types (histocompatibility leucocyte antigen) and islet cell antibodies have not been found (Freinkel,1977).

III - Secondary diabetes:

Including diabetes mellitus associated with certain conditions or syndromes. In this subclass diabetes occurs in relation to other disease state of pancreatic diseases, hormonal, drug or chemical induced, insulin receptor abnormalities, genetic syndromes and other causes.

ETIOLOGIES OF DIABETES MELLITUS

Most diabetic persons are classified as having one of two major types of diabetes with correspondingly different causes.

It has been found that genetic, environmental and immunologic factors separates IDDM from NIDDM.

I - Type I diabetes mellitus (IDDM):

The disorder previously known as "juvenile diabetes" is now identified as type I,or insulin-dependent diabetes mellitus (IDDM).Its development is seemingly multifactorial as genetic factors, viral infections, and immunological factors. Its genetics and immune characteristics seem to be closely interrelated. (Lawrence **and Amadeo,** 1984).

*** Genetic transmission:**

Genetic predisposition to type I diabetes is most pronounced in monozygotic twins. It is known that about 50 percent of them exhibit concordance, i.e. if an identical twin has diabetes, the other twin will invariably develop diabetes (Potemkin,1989).

There is evidence of an association between certain HLA antigens and type I diabetes .

The relationship of certain human lymphocyte antigens (HLA) to specific diseases can be best described by appreciation of the fact that approximately 95 % of patients with ankylosing spondylitis have the HLA subtype BW 15. Exhaustive analysis has disclosed that HLA - B 8 and HLA - BW 15 are highly correlated with IDDM in whites and in natives of India.

The HLA's are present on the surface of all nucleated cells, and their type is controlled by loci on the short arm of chromosome 6.

It is believed that the HLA system directs both host defense and self-recognition. The fact that the presence of HLA-B 7 is negatively correlated with