CARDIAC PERFORMANCE STUDY IN CHILDREN WITH INSULIN DEPENDENT DIABETES MELLITUS (IDDM)

T H E S I S

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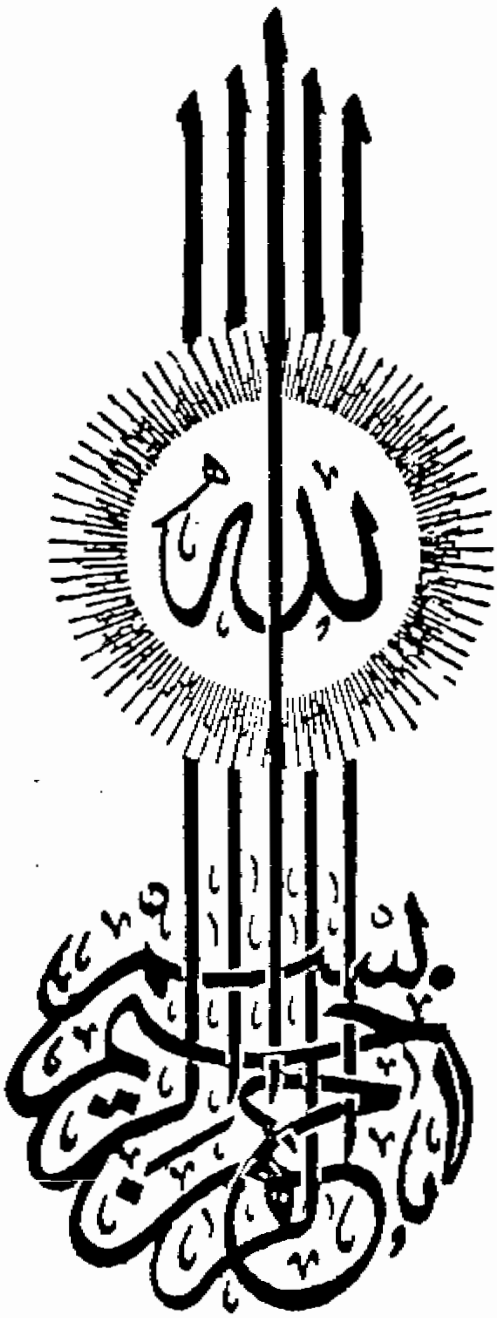

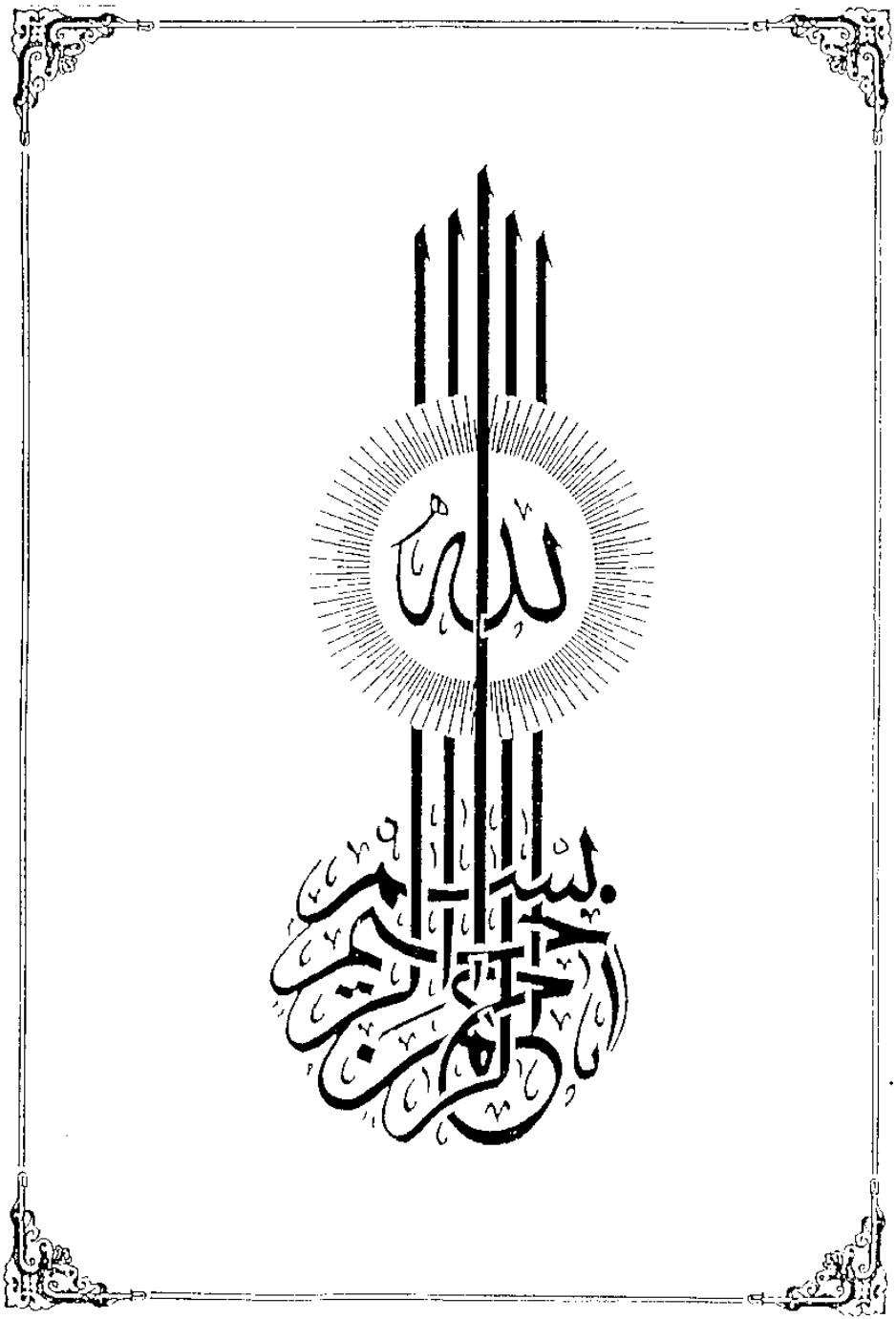

CONTENTS

Page

- INTRODUCTION AND AIM OF THE WORK 1
- REVIEW OF THE LITERATURE 4
  - Diabetes Mellitus 4
    - Classification 6
    - Prevalence - Incidence of IDDM 12
    - Aetiological factor in IDDM 14
    - Complications of IDDM 18
    - Glycosylated hemoglobin 23
  - Juvenile Diabetes and the Heart 24
    - Macrovascular disease (Atherosclerosis and diabetes mellitus 26
    - Coronary artery disease 28
    - Arterial pulse wave velocity 29
    - Innervation of the heart 29
    - Diabetic neuropathy 30
    - Microangiopathy, cardiomyopathy 33
    - Cardiomyopathy in fetus 37
  - Echocardiography 39
    - M-mode examination 40
    - Two-dimensional examination 46
    - The advantages and disadvantages of M-mode and 2D echocardiography 54
    - Echocardiographic evaluation of left ventricular function 55
  - Exercise Electrocardiography 73
    - Pathophysiologic consideration of Exercise ECG test 73
    - Indication for Exercise ECG test in children 75
    - Exercise ECG test contraindication 77

CONTENTS (Cont'd)

Page

- Physiologic response to exercise 77
- Abnormal response to exercise 80
- Protocols for the exercise ECG test 87
- Preparation for the exercise treadmill ECG test 88
- End-point to terminate exercise test 89

- MATERIAL AND METHODS 91
  - History and full examination 91
  - Laboratory Investigation 92
    - Fasting blood glucose 92
    - Glycosylated hemoglobin 92
  - Cardiac Investigation 92
    - X-ray chest (P.A.) 92
    - Resting electrocardiogram 92
    - Complete M-mode and two-dimensional echo-cardiography 92
    - Treadmill exercise test (Bruce Protocol). 94

- RESULTS 103

- DISCUSSION 149

- SUMMARY AND CONCLUSION 162

- REFERENCES 166

- ARABIC SUMMARY.

List of Abbreviations

ASCVD	: Atherosclerosis cardiovascular abnormalities.
HbA_{1c}	: Glycosylated hemoglobin.
IGT	: Impaired glucose tolerance.
N.D.D.G.	: National Diabetes Data Group.
OGTT	: Oral glucose tolerance test.
P.A.S +ve	: Periodic acid Schiff positive.
P.V.Cs	: Premature ventricular contraction
P.W.T.	: Posterior wall thickness.
$\triangle$ R-ST index	: R wave + ST segment.
R.W.A.	: R-wave amplitude.
S_3 , S_4	: Sound 3 , sound 4.
S.V.T	: Supraventricular tachycardia.
S.W.T	: Septal wall thickness.

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INTRODUCTION AND AIM OF THE WORK

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Diabetes mellitus is the most common endocrine and metabolic disorder of childhood and adolescence with important consequences on physical and emotional development (Sperling, 1983).

Morbidity and mortality stem from metabolic derangement and from long term complications that affect small and large blood vessels resulting in retinopathy, nephropathy, neuropathy, ischemic heart disease and arterial obstruction with gangrene of extremities (Tamborlane and Sherwin, 1983).

Recent studies suggest that the pathophysiology in target organs such as the eye, kidney, nerve, heart and peripheral vessels may well begin as early as one to two years following the onset of the disease (Knowles, 1978).

The clinical feature of heart disease in the diabetics lies in three categories:-

1- Macroangiopathy (coronary atherosclerosis).

2- Autonomic neuropathy.

3- Cardiomyopathy.

Atherosclerosis occurs at an earlier age and to a greater degree in diabetics, the abnormal carbohydrate and lipid profile often result in hypertriglyceridemia and hypercholesterolemia, this

coupled with hyperglycemia-induced endothelial dysfunction, increased platelet adhesiveness and impaired intracellular degradation of low-density lipoproteins (Olefsky, 1974), may all contribute to the development of atheroma and subsequent macroangiopathy of atherosclerosis (Cerami and Brownlee, 1981).

Autonomic neuropathy has specific effects on the cardiovascular system, e.g. tachycardia at rest and loss of beat to beat variation with respiration due to parasympathetic damage. Postural hypotension and abnormal blood pressure response to hand grip due to sympathetic dysfunction (Campbell et al, 1975). Painless myocardial infarction due to damage of vagal cardiac nerves and also there is denervation hypersensitivity to catecholamine leading to serious arrhythmias (Kannel and McGhee, 1979).

Cardiomyopathy represented by cardiomegaly, biventricular failure and gallop rhythm have been described in diabetics in absence of coronary heart disease, hypertension or valvular lesion (Shapiro, 1984).

Biochemical studies indicate that hyperglycemia or insulin deficiency produce alteration in vascular basement membrane composition as well as deposition of (P.A.S) positive glycoprotein

in the interstitium of the myocardium and perivascular fibrosis (Regan et al, 1978), leading to decrease ventricular compliance resulting in cardiomyopathy and ventricular stiffness which in turn lead to decrease stroke volume and increase in left ventricle-end-diastolic pressure at rest (Shapiro, 1982).

The aim of our work is to evaluate the cardiac performance in children with insulin-dependent-diabetes mellitus by the use of M-mode and two-dimensional echocardiography and exercise stress testing.

REVIEW OF LITERATURE

DIABETES MELLITUS

Diabetes mellitus is the most common endocrine and metabolic disease in childhood that has important consequences on physical and emotional development (Sperling, 1983).

It has become increasingly clear that the term 'diabetes mellitus' encompasses a syndrome rather than a single well defined disease entity. The evidence which establishes diabetes mellitus as a heterogenous group of independent disease has been reviewed recently. Within this group the insulin dependent type of diabetes mellitus (IDDM) stands out as a nosological entity in its own characteristic clinical picture, distinctive pathological findings in the islet of Langerhans and particular genetic and immunological features (Zonna and Rimorin, 1976).

Diabetes mellitus is considered a complex syndrome characterized by:-

1- Chronic hyperglycaemia secondary to deranged secretion or action of insulin (Wellborn, 1984).

2- Specific microvascular complications including thickening of capillary basement membrane, retinopathy and nephropathy.

3- Macrovascular disease, i.e. accelerated atherosclerosis and a variety of other complications, neuropathy, complicated pregnancy and increased tendency to infection.

Insulin Dependent Diabetes Mellitus (IDDM)

IDDM defines a group of patients who are usually but not necessarily under 30 years of age at the time of diagnosis. They generally present with an accelerating history of glucosuric symptoms for less than three months. They are thin and almost invariably exhibit weight loss. Only rarely are such patients discovered by testing for diabetes when they are asymptomatic, if so, they may decompensate soon after (Fajans et al., 1976). This defines their state of absolute insulin dependency (Genuth, 1982). Only 10% of patients of IDDM have either a diabetic parent or a diabetic sibling (Fajans, Cloutier and Crowther, 1978).

Functionally, IDDM is characterized by insulinopenia (Genuth, 1982). Fasting plasma insulin levels are low and there is little or no response to challenge with glucose amino acids, tolbutamide, glucagon or other beta cell stimulants. Anatomically, the islets are small and devoid of beta cells, though hyperplasia of other islet cells that produce glucagon, somatostatin and pancreatic polypeptide is often seen (Gepts, Demey and Marichal-Pipeleers, 1977).

A well defined subgroup of youthful onset diabetics, sometimes known as MODY (Maturity Onset Diabetes of Youth) or

NIDDY (Non Insulin Dependent Diabetes of Youth) may be diagnosed in their teens, though these patients are usually treated with insulin. They are able to survive without it (Tattersal, 1974; Fajans, Cloutier and Crowther, 1978).

In contrast, clinical onset in latter life by no means, excludes a truly insulin dependent state.

CLASSIFICATION:

In the past, differences were noted between forms of diabetes secondary to other well-known disorders mainly endocrinopathies and forms that have no clear correlation with other diseases and for this reason, are called primary or idiopathic diabetes. More recently, studies on the families of diabetic patients, studies of identical twins, the evaluation of autoimmune phenomena, the study of cell mediated immunity and the genetic findings have clearly separated at least two substantially different forms within primary diabetes. In the last few years, different classifications of diabetes have been reported (Bottazzo and Doniach, 1976; Cudworth and Woodrow, 1976; Irvine, 1977).

A major problem at present is that no classification is satisfactory for both the clinician and the researcher, so in 1979, the National Diabetes Data Group (NDDG) developed together with