CALCIUM HOMEOSTASIS IN INSULIN DEPENDENT DIABETES

THESIS
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BY

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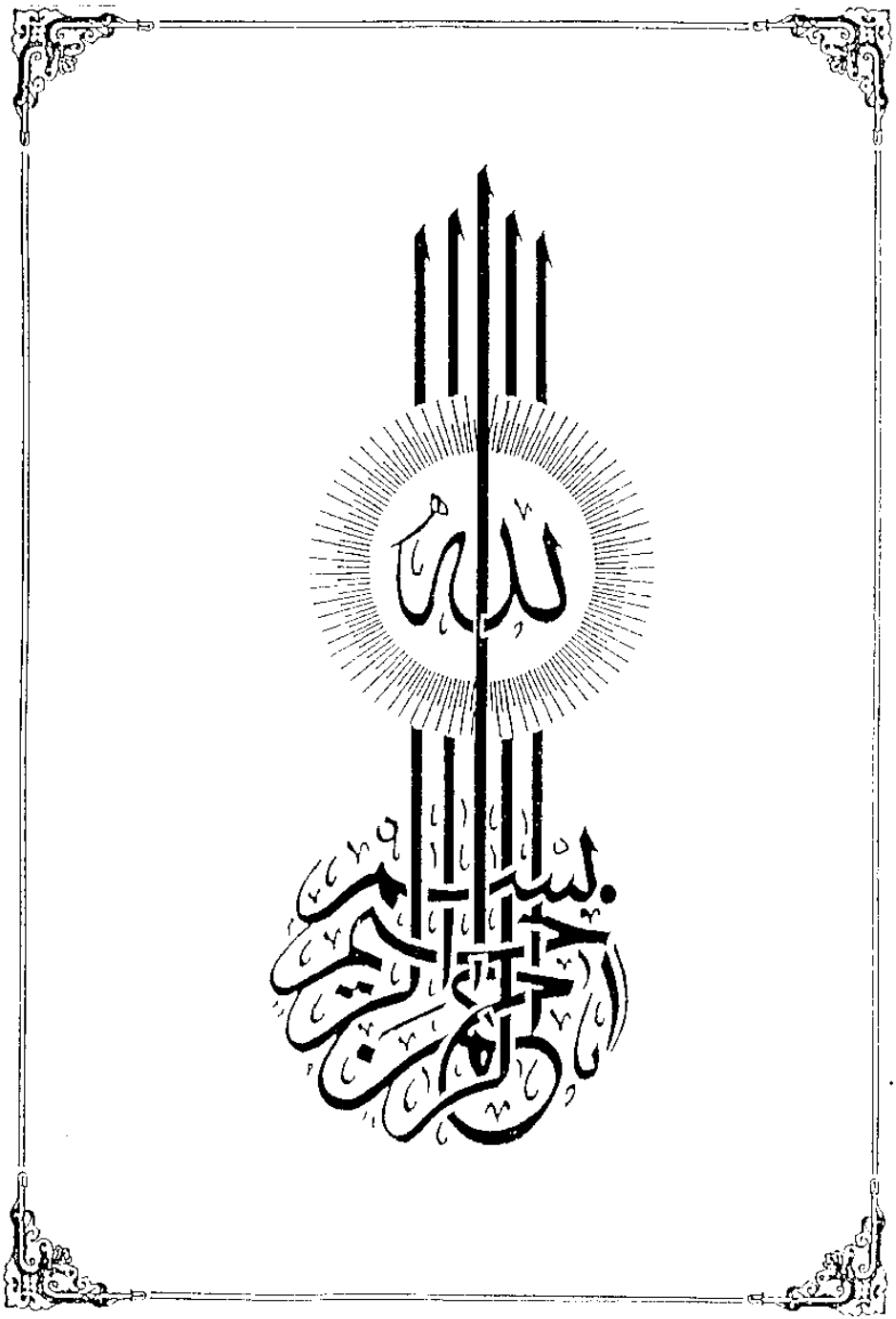

LIST OF ABBREVIATIONS

D.M.	DIABETES MELLITUS
HLA	HISTOCOMPATIBILITY ANTIGENS
IDDM	INSULIN DEPENDENT DIABETES MELLITUS
ICT	IMMUNOREACTIVE CALCITONIN
IPTH	IMMUNOREACTIVE PARATHYROID HORMONE
ICA	ISLET CELL ANTIBODIES

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Introduction

INTRODUCTION AND AIM OF THE WORK

Despite the wealth of information available concerning the variety of systemic complications of diabetes mellitus, little is known about the effect of this disease on the metabolism of minerals and the integrity of bone. In recent years it has become apparent that involvement of the skeletal system must be regarded as another complication of diabetes **(Rosenbloom et al., 1977).** Alteration in mineral metabolism are associated with changes in skeletal morphology in the growing rat with experimental diabetes **(Brown, 1977 and Schedl, 1978).**

The role of diabetes as a cause of a metabolic bone disease resulting in generalized decrease in bone mass (osteopenia) attracts our attention to study the Ca, and P, homeostasis in IDD to clarify the disorder of Ca, and P, metabolism in IDD and to define abnormalities that might account for osteopenia of diabetes.

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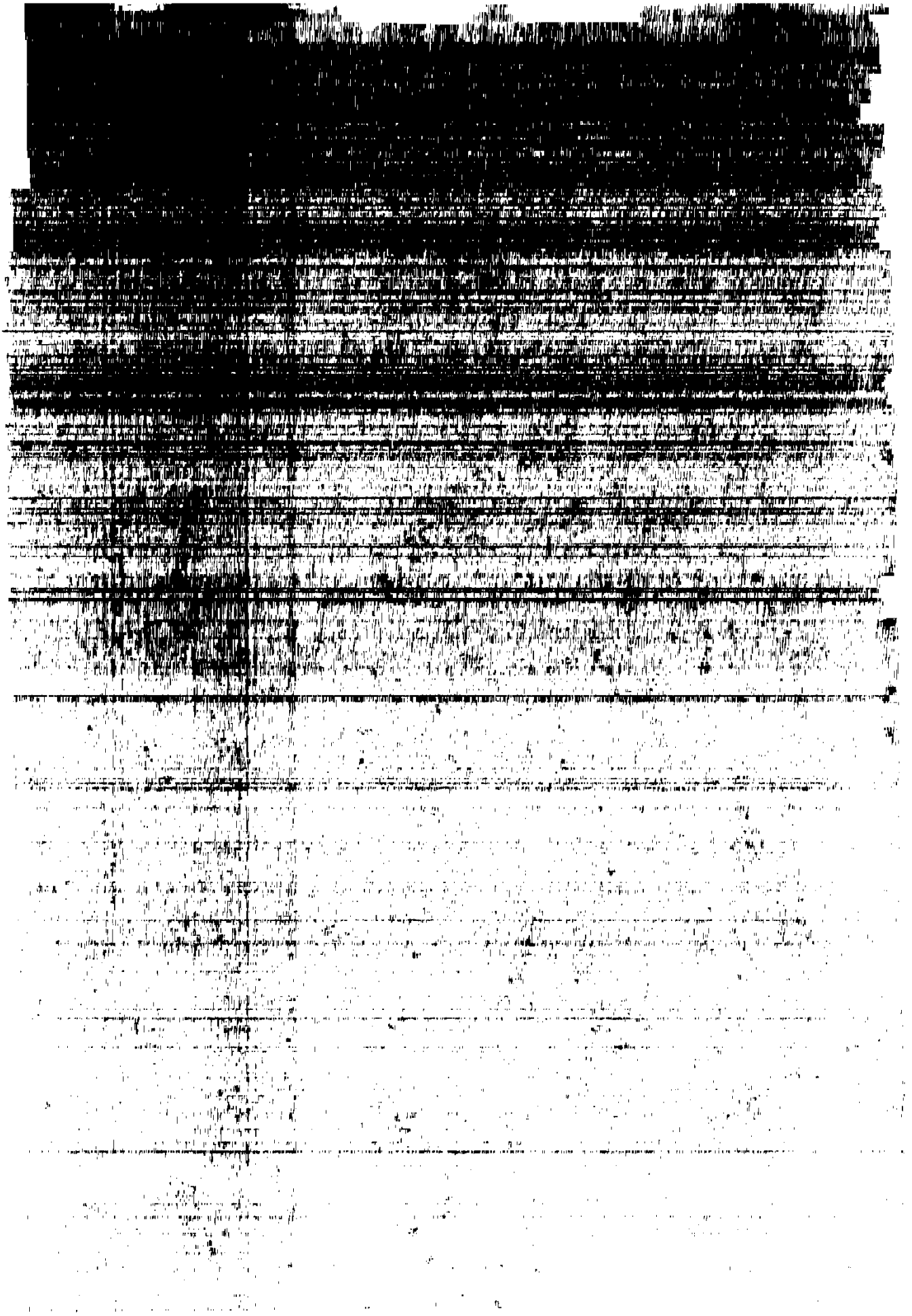
Review of literature



DIABETES MELLITUS (D.M.)

Definition:

Diabetes mellitus is not a single disease but rather a clinical syndrome characterized by inappropriately elevated fasting and/or postprandial blood glucose with accelerated fat and protein catabolism. The syndrome is also characterized by the development of long-term microvascular, macrovascular, and neuropathic changes which appear as peripheral sensory and motor defects, autonomic nervous system dysfunction, segmental dysfunction and abnormalities of schwann cells (Porte and Halter 1981). This D.M. clinical syndrome results from a large variety of etiologic and pathogenetic mechanisms.

Classification of Diabetes Mellitus:

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. Within the latter forms of diabetes there are clinical differences in the onset and evolution of the disease that have been more clearly

assessed. More recently studies on the families of patients, studies of identical twins, the evaluation of autoimmune phenomena particulary the antibodies against the islet cell cytoplasm, the study of cell mediated immunity and the genetic finding have clearly separated at least two substantially different forms within primary diabetes **(DiMario et al., 1980).**

In (1979) National diabetes Data Group, developed together with the main associations for the study of diabetes, a new classification of the disease **(National Diabetes Data Group, 1979).** The aim was to give diabetologists a uniform framework to conduct clinical and epidemiological research or to follow therapeutic guidelines **(Table 1).**

Idiopathic	Secondary
- Insulin-dependent (type I)	- Pancreatic trauma, disease or resection.
- Non-insulin-dependent (type II).	- Hormone-induced. - Drugs and chemical agents.
- Maturity-onset diabetes of youth (MODY).	- Genetic syndromes. - Insulin receptor abnormalities.
	- Other types.

This classification divides primary diabetes according to insulin dependence. Nevertheless the sole

Criterion of insulin dependence may be misleading because there are many non insulin-dependent subjects that are treated with insulin for various reasons. Furthermore, among the non-insulin dependent diabetic patients there is a small group that within a few months or years of diagnosis develop a clear insulin dependence. To overcome these and other limits the same group proposed a parallel classification for research purposes. The detection of islet cell antibodies (ICA), the association with organ specific autoimmune disorders, HLA typing and the mode of inheritance are the main criteria **(Table II).** This classification also has many theoretical and practical limits, the most important one is that only a few diabetic clinics are able to perform genetic and immunological studies.

Table II

Provisional research subclassification of type I diabetes (National Diabetes Data Group 1979, modified)

Diabetes Mellitus			
Association with organ specific auto immune disease or autoimmune phenomena.		Presence of islet cell antibodies (in relation to onset of insulin dependency).	Other characteristics that offer promise of being used to subclassify diabetes.
Insulin-dependent type (IDDM)			
Subclass a	Positive	Usually persistent	Possible viral aetiology prevalence of HLA types (elevated or reduced relative to general population), such as DR_2, DR_3, DR_4, B_8, B_{15} etc; antibody response to exogenous insulin
Subclass b	Negative	Usually transient.	
Subclass c	Negative	Undetected.	

INSULIN-DEPENDENT DIABETES "TYPE I" (IDD)

Prevalence and incidence:

The insulin dependent group represent about 5-10 percent of the total diabetic population and the non-insulin dependent group about 85 to 90 percent **(Benett, 1976 & Genuth, 1982).** Insulin-dependent diabetes occurs very rarely in Pima Indians and somewhat less often in Japanese and perhaps in American blacks than in Caucasians **(La Porte et al., 1981).** It seems to be rare in many African and Asian population **(Porte and Halter, 1981).** Its incidence in European studies is around 10 per 100,000 **(Christu et al., 1977).** In the Arab countries very few studies on the prevalence of **DM** have been carried. In Tunisia, the fasting blood glucose was measured in 9177 persons. 1.2% of the sample was known as diabetics and 1% were newly diagnosed. The prevalence increased above the age of 4 years **(Ben Kalifa 1978).** Few studies considering the prevalence of **IDDM** in Egypt have been carried.

In **(1981) El Taweel** reported that the prevalence rate of **IDDM** in the age category of 6-13 years of

Egyptian children chosen from primary schools in Cairo and Guiza is 0.8 per 1000. In Benha the prevalence rate is 0.9 per 1000 was reported among school children **(Zaki, 1982).** **El-Bayadi (1983)** reported that the prevalence rate in El Ahram district in Guiza 0.25 per 1000. In Egypt, the incidence of **IDDM** was estimated among infant of Mounira children hospital and it was reported to be 0.2% of hospital admission surveyed during a 4 year period **(Gabr & Abdel Salam, 1962).**

There is a linear relationship between age and prevalence of diabetes i.e. the prevalence rate is rising with increasing in age **(Kyllo, 1978; Dahlquist et al., 1982).** The male preponderance in young age and female preponderance in the older age is also a general agreement with many previous reports **(Gamble, 1980 & Joner, 1981).** It has been reported that **IDD** is rare in the first few months of life, its frequency is increasing abruptly at about nine months of age. The cause of this rise is uncertain, however, it coincides with increasing exposure to many dietary and other environmental factors. There is a similarity between this age distribution and that of most infections which are rare before the age of