Nerve Conduction Studies and Median Nerve Somatosensory Evoked Potential in Egyptian Diabetic Patients

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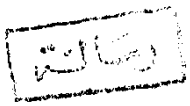

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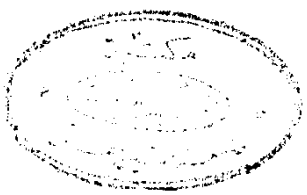

بسم الله الرحمن الرحيم

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خلق الإنسان من علق اقرأ وربك الأكرم
الذى علم بالقلم
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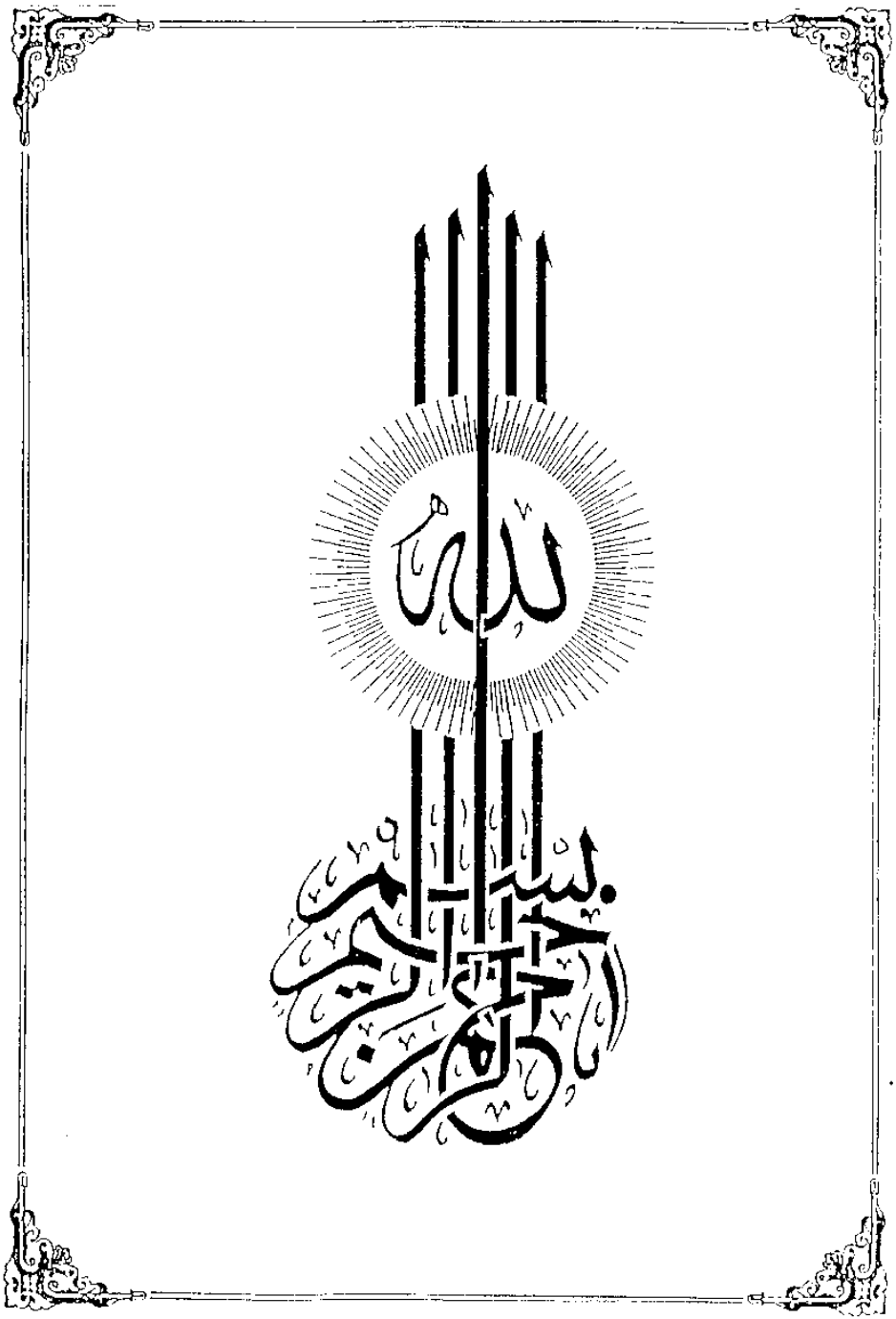
صدق الله العظيم

سورة العلق ١-٥



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Introduction

INTRODUCTION

Diabetes mellitus is a common metabolic disorder. It comprises an etiologically and clinically heterogeneous group of hyperglycemic disorders. The hyperglycemia is a consequence of relative or absolute deficiency of insulin . It is associated with a set of complications including mainly neuropathy, retinopathy, nephropathy and macro vascular disease *(Unger and Foster,1992)*.

Peripheral neuropathy is the most frequent complication of diabetes mellitus, approximately 50% of patients have signs of peripheral neuropathy *(Palumbo et al, 1978; Melton and Dyck, 1987)*. Peripheral neuropathy has been extensively studied clinically pathologically and electrophysiologically.

Peripheral diabetic neuropathy is clinically defined as symptoms of peripheral nerve involvement associated with abnormal signs and or abnormal objective measurements (such as, abnormal nerve conduction studies) without evidence of other causes of neuropathy, subclinical neuropathy is defined by the same criteria but without the presence of symptoms *(Bays and Pfeifer, 1988)*.

Pathological studies have shown that peripheral neuropathies are mainly demyelinating but some are due to axonal degeneration, often with secondary demyelination. In demyelination neuropathies nerve conduction is usually markedly delayed, while in axonal degeneration the surviving axons conduct at a normal rate but the amplitude of evoked muscle or sensory potentials is reduced *(Dyck et al., 1983)*.

There have been only a few studies of central nervous system involvement in diabetes, classic text books of diabetologia list as central nervous system abnormalities in diabetes only diabetic coma and a greater liability to vasculopathy .

However, Reske-Neilson and *Lundbeck (1968)*, in an autopsy study of 3 diabetics, found diffuse degeneration of nerve fibers in brain, brain stem and cerebellum. This has recently been confirmed by *Franceschi et al,(1984)* who reported altered memory function in diabetics.

Spinal cord disease in diabetes has been described as diabetic myelopathy *(Garland and Taverner, 1953; Slager, 1978)* and posterolateral sclerosis *(Relkin and Esseesse,1976)*. It is usually attributed to damage of the spinal ganglion cells secondary to ascending peripheral neuropathy rather than to a true primary myelopathy *(Gupta and Dorfman, 1981)*. Until a few years ago there were no techniques for adequate functional study of the spinal cord. Somatosensory evoked potential (SEPs) following both stimulation of upper or lower limbs can provide information about conduction in both peripheral and central afferent pathways.

Aim of the Work

Aim of the Work

The aim of our work is to conduct a clinical and electrophysiological study on Egyptian diabetic patients in order to detect.

- Incidence of central and peripheral nervous affection in both upper limbs

- The type of peripheral nerve affection.

- Localization of central affection.

DIABETES MELLITUS

Diabetes is generally defined by a particular degree of hyperglycemia resulting in a complex metabolic disorder with various long term sequelae. It is however, difficult to produce a single binding definition because of the different aetiologies and varying severity and manifestations of diabetes. In diabetes, the fundamental defect is in insulin secretion and or action. In the classical young onset form of the disorder, there is near-total insulin deficiency, with inevitable widespread metabolic changes. In the older-age onset form, there is diminished and or delayed insulin secretion in response to glucose, combined with varying degree of diminished effectiveness of circulating insulin. When there is associated obesity, insulin resistance predominates. Diabetes can therefore be defined as a state of diminished insulin action, due to its decreased availability or effectiveness, in varying combinations *(Alberti and Hockaday, 1987)*.

Classification:

The World Health Organization (WHO, 1980) classified diabetes into:

1- Insulin dependent diabetes mellitus (IDDM or type I diabetes)

2- Non-insulin-dependent diabetes mellitus (NIDDM) or type II diabetes:
   a- Obese NIDDM (about 80%).
   b- Non obese NIDDM (about 20%).

3- Impaired glucose tolerance (IGT).

4- Secondary diabetes: Diabetes may form a part of other conditions and syndromes:-

A. Pancreatic disease:

These include pancreatitis, pancreatic calculi with fibrosis, cystic fibrosis, cancer of the pancreas, hemochromatosis and toxic damage to the pancreas.

B- Hormonal overactivity:

These include pheochromocytoma, acromegaly, cushing syndrome, glucagonoma, somatostatinoma, and aldosternoma.

C- Drug or chemically induced condition:

These include thiazides, diazoxide, and streptozotocin as well as hormonally active agents such as glucocorticoids, growth hormone, progestins and oestrogens.

D. Insulin receptor abnormalities:

These include congenital lipodystrophy, and acanthosis nigricans associated with virilization.

E- Genetic Syndromes:

These include certain inborn errors of metabolism, insulin resistant syndromes and hereditary neuromuscular disorders.

5- Gestational diabetes: The onset or diagnosis of diabetes or impaired glucose tolerance occurs during pregnancy .

Insulin Dependent Diabetes Mellitus (IDDM):

Type I diabetes is a chronic autoimmune disease associated with selective islet ß cell destruction that leads to IDDM *(Eisenbarth, 1989).*

Family studies:

Familial aggregation of type I IDDM is uncommon. Less than 4% of the parents and 6% of the siblings of a patient with IDDM had diabetes *(Simpson, 1962).* In another study diabetes was present in 11% of parents and 11% of siblings *(Taltersall and Fajans, 1975).* Low concordance rate of 50 % or less for IDDM has been reported in monozygotic twins *(Barnett et al, 1981).*

Aetiology and pathogenesis of IDDM:

Genetic predisposition:

Over 90% of white IDDM patients have either D3-DR3 or D4-DR4 antigens; 55% to 60% have both DR3 and DR4 *(Cudworth and Woodrow, 1975).* On the other hand, D2-DR2 positive subjects enjoy striking protection from IDDM, referred to as a resistance axis *(Cudworth et al, 1980).*

Environmental factors:

Although the set of IDDM frequently coincides with or follows infection with mumps, rubella, cytomegalic, measles, influenza, encephalitis, myocarditis, poliomyelitis and Epstein-Bar viruses *(Notkens, 1979).* It has been impossible to fix any particular viral agent or group of agents as regular forerunners of the disease. It could equally be argued that the probable link between viral infection and subsequent development of type I diabetes is nonspecific through the generalized stress of infection rather than a more direct consequence of the infective agent *(Alberti and Hockaday, 1987).*

3- Autoimmune mechanisms:

The evidence that IDDM is an immune-mediated disease can be summarized as follows:

a) It is linked with class II antigens known to be associated with auto immune disease *(Cudworth and Woodrow, 1975).*

b) IDDM frequently occurs with other forms of immune endocrinopathy, such as Hashimoto's thyroiditis, adrenal insufficiency, pernicious anaemia and myasthenia gravis *(Maccuish and Irvine, 1975).*

c) A very early lesion in IDDM is an infiltration of lymphocytes in the islets of langerhans *(Gepts, 1965).*

d) Islet cell antibodies directed against both cytoplasmic and cell surface determinants are present in a high percentage of IDDM patients at the time of diagnosis *(Bottazzo et al, 1974).*

Non-Insulin-Dependent Diabetes Mellitus (NIDDM):

Type II or non insulin dependent diabetes mellitus is the most common cause of hyperglycemia in adult population. Although usually described as a single disease, type II diabetes is more likely a group of related syndromes often associated with obesity and characterized by fasting and or post prandial hyperglycemia with resistance to ketoacidosis. Unlike the type I diabetes, the type II diabetes is not dependent on insulin therapy for survival but may receive insulin for better control of blood sugar *(Kahn, 1989).*

Family studies:

Thirty-eight percent of siblings and one third of the off spring of individuals with NIDDM exhibit diabetes or abnormalities in glucose tolerance *(Kobberling, 1971).* Concordance of identical twins for type II NIDDM is 90 to 100% compared to half or less in type I IDDM *(Barnett et al, 1981).*

Aetiology and pathogenesis of NIDDM:

Genetic predisposition:

There is no association between HLA and NIDDM in whites *(Unger and Foster, 1985).* NIDDM is assumed to be a multigenic disorder with a threshold rather than a mendalian trait. In multigenic diseases the individual genetic factors each contribute additively and some may be more important than others. For example, there may be a major locus in NIDDM with relatively few contributing loci. According to this model, NIDDM develops when the susceptibility threshold is exceeded *(Rich, 1990).*

Environmental factors:

NIDDM is considered to have a multifactorial etiology that involves multigenic and environmental factors. The environmental factors contribute to the additivity and to reaching the threshold along with other genetic variables *(Granner and O'Brien, 1992).* Presumably the major environmental factor is greater food availability which in turn predisposes to obesity *(Zimmet, 1979).* NIDDM results from imbalance between

insulin sensitivity and insulin secretion. The earliest detectable abnormality in NIDDM is an impairment in the body's ability to respond to insulin. Because the pancreas is able to appropriately augment its secretion of insulin to offset the insulin resistance, glucose tolerance remains normal. With time, however the ß-cell fails to maintain its high rate of insulin secretion and the relative insulinopenia (i.e, relative to the degree of insulin resistance) leads to the development of impaired glucose tolerance and eventually overt diabetes mellitus *(Defronzo et al, 1992).*

Presenting features of diabetes mellitus:

The classic symptoms of hyperglycemia are polyuria, thirst, weight loss and lassitude. In insulin-dependent diabetes mellitus (IDDM), weight loss may be severe while, in non insulin dependent diabetes mellitus (NIDDM), there may be no significant weight loss at diagnosis. Nocturnal frequency is often two to four times, and thirst severe enough for patients to drink at night. In women pruritis vulvae is a frequent symptom. Other very non specific symptoms commonly complained of are the appearance or exacerbation of cramps in the calves or feet particularly at night, and tingling in the fingers *(Alberti and Hockaday, 1987).*

Complications of diabetes mellitus include:

- Atherosclerosis.
- Cardiomyopathy.
- Dermopathy.
- Diabetic foot syndrome.
- Nephropathy.
- Diabetic retinopathy.
- Diabetic neuropathy.

Diabetic neuropathy affects somatic and autonomic neurons. An increased liability to cerebral and spinal arterial disease is widely accepted. Peripheral neuropathy is both extremely common, highly symptomatic and annoying *(Alberti and Hockaday, 1987).*