THE EFFECT OF INSULIN LIKE GROWTH FACTOR I AND GLYCEMIC CONTROL IN INSULIN DEPENDENT DIABETES MELLITUS

THESIS

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بسم الله الرحمن الرحيم

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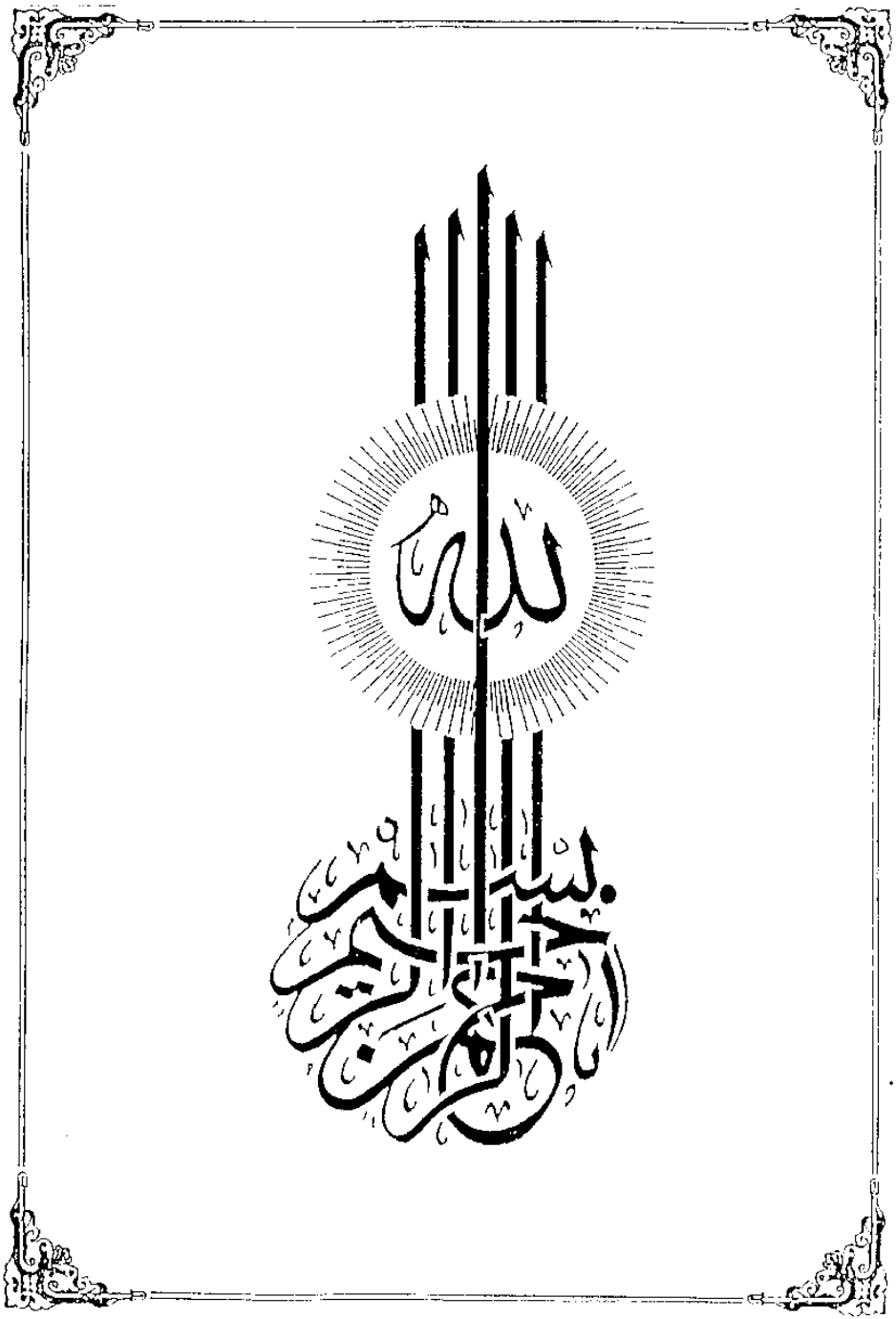

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Sahar Assaad

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EDTA : Ethyene Diamine tetra-acetate

Hb : Hemoglobin

HbA1 : Glycosylated Hb

HbA1C : Fraction C

IDDM : Insulin-dependent diabetes mellitus

IGF-I : Insulin like growth factor

Introduction

Puberty is a time of dramatic hormonal and physical changes. Under the influence of pituitary gonadotropins, gonadal production of testosterone or estrogen leads to the development of secondary sexual characteristics and the attainment of full reproductive potential ***(Luna et al., 1983).***

Additionally, sexual maturation is normally characterized by a marked increase in linear growth velocity. The pubertal growth spurt is dependent upon both the sex steroids and GH. GH does not, however, appear to act directly on growing tissue, but rather, its actions are mediated through IGF-I ***(Smith, 1977).***

IGF-I which is a circulating basic peptide was found to be of lower levels in diabetic patients ***(Tan and Baxter, 1985).***

Beside, linear growth of diabetic children in poor metabolic control is decreased when compared to that of well-managed diabetic children ***(Jackson and Kelly, 1946).***

Aim of the work:

The aim of this work is to assess the effect of puberty and glycemic control on plasma IGF-I levels and growth velocity in insulin dependent diabetes mellitus.

Diabetes Mellitus

Definition:

Diabetes mellitus (DM) is a syndrome of disturbed energy homeostasis caused by deficiency of insulin or of its action and resulting in abnormal metabolism of carbohydrate, protein and fat. It is the most common endocrine-metabolic disorder of childhood and adolescence with important consequences on physical and emotional development ***(Sperling, 1992).***

DM can also be defined as a heterogenous primary disorder of carbohydrate (CHO) metabolism with multiple etiologic factors that generally involve absolute or relative insulin deficiency or insulin resistance or both. All causes of diabetes ultimately leads to hyperglycemia, which is the landmark of this disorder syndrome ***(Olefsky, 1992).***

The disease is characterized by metabolic abnormalities; by long-term complications involving the eyes, kidneys, nerves and blood vessels; and by a lesion of the basement membranes demonstrated by electron microscopy ***(Foster, 1991).***

Classification of diabetes mellitus

A classification of diabetes mellitus is given in the table IA. The basic categories are those recommended by the National Diabetes Data Group except for division into primary and secondary types.

Primary implies that no associated disease is present while in secondary category some other identifiable condition causes or allows a diabetics syndrome to develop. Insulin dependence in this classification is not equivalent to insulin therapy rather, the term means that the patient is at risk for ketoacidosis in the absence of insulin.

The term type I is often used as a synonym for insulin-dependent diabetes (IDDM) and type II diabetes has been considered equivalent to non insulin-dependent diabetes mellitus (NIDD). This is probably not ideal and better refer type 1 and type 2 to immune mediated and non-immune mediated respectively.

Thus according to this classification, three major forms of 1ry diabetes would be recognized:
(1) Type 1 insulin dependent diabetes.

Type I insulin dependent diabetes mellitus (IDDM)

Type I is a severe form of diabetes mellitus and is associated with ketosis in the untreated state. About 10-20% of diabetes in North America and Europe are of the insulin dependent type. It is most common in young individuals but occurs occasionally in non obese adults. It is a catabolic disorder in which circulating insulin is virtually absent, plasma glucagon is elevated and the pancreatic β cells fail to respond to all known insulinogenic stimuli. In the absence of insulin, the 3 main target tissues (liver, muscle and fat) not only fail to appropriately take up absorbed materials but continue to deliver glucose, amino acids and fatty acids into the blood stream from their respective storage depots ***(Eisembrath, 1987).***

Subgroups of type I diabetes:

In Britain, a subclassification of type I diabetes has been suggested. One subgroup, termed Ia accounts for 80% of type I diabetes. These patients have islet cell autoantibodies only transiently, at the onset of their disease; they seldom have any other associated autoimmune phenomena. A viral infection appears to be mainly responsible for the β cell destruction in these patients. The most common HLA type in this subgroup are B15 and DR4.

Subgroup Ib accounts for the remainder of insulin dependent diabetic patients. These patients have islet cell autoantibodies that tend to persist in high titres. Associated autoimmune disorders of the thyroid and adrenal cortex occur frequently; hypogonadism and pernicious anaemia are also found. Immune destruction of pancreatic β cells appear to be responsible for the development of the disease. Most of these patients are females, and the most frequent HLA types are HLA-B8 and HLA-DR^3.

Incidence:

In Egypt, the incidence varied greatly in the different series, 0.2% by ***Gabr and Abdel-Salam (1962)***, 0.8 per 1000 by ***El-Taweel (1981)***, 0.26 per 1000 by ***El-Bayadi (1983)***, 1.21 per 1000 in 1988 and 1.09 per 1000 in 1990 ***(Salem et al., 1990).***

Abroad, an incidence of 9.0 out of 100.000 children under 19 years of age with type I (insulin dependent) diabetes was detected in Toronto during a 2 year perspective study. The incidence of type I diabetes in Toronto is similar to other North American studies. Incidence in other countries vary from 3.7 out of 100.000 in France to 20 out of 100.000 in Finland.

The higher incidence in Finland and the apparent low incidence in France may represent real difference in genetic susceptibility and environmental exposure of a study population ***(Ehrlich et al., 1982).***