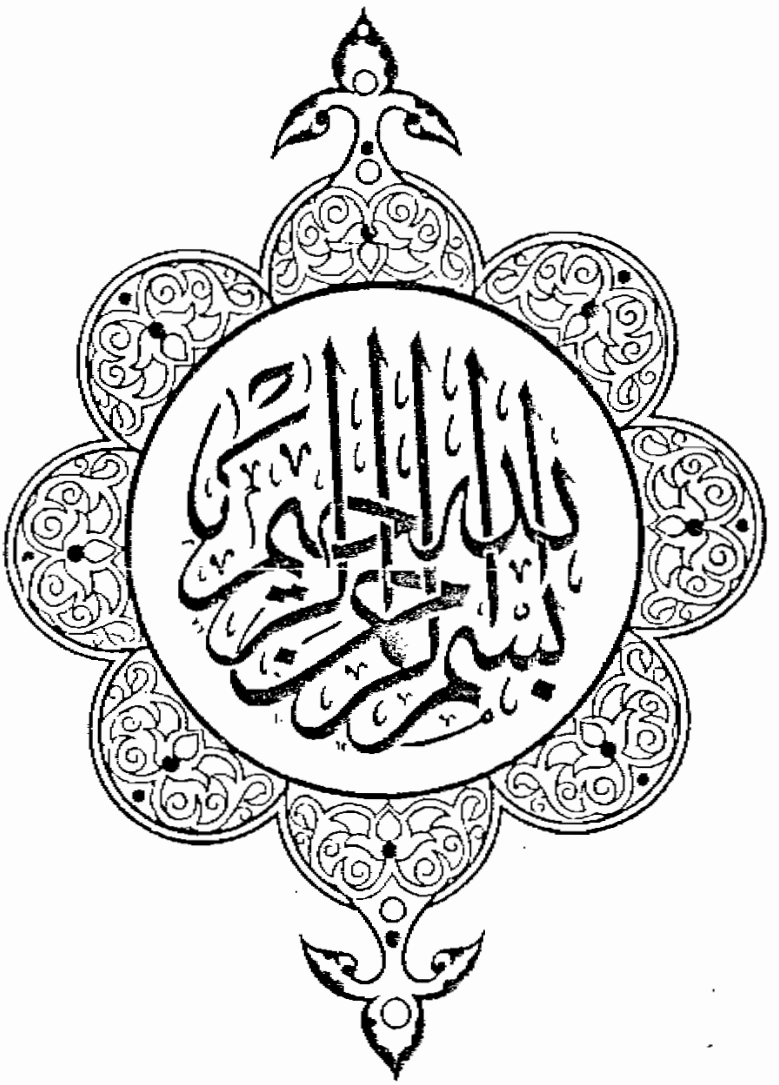

SERUM INSULIN IN TYPE II DIABETICS AND ITS RELATION TO DURATION

THESIS

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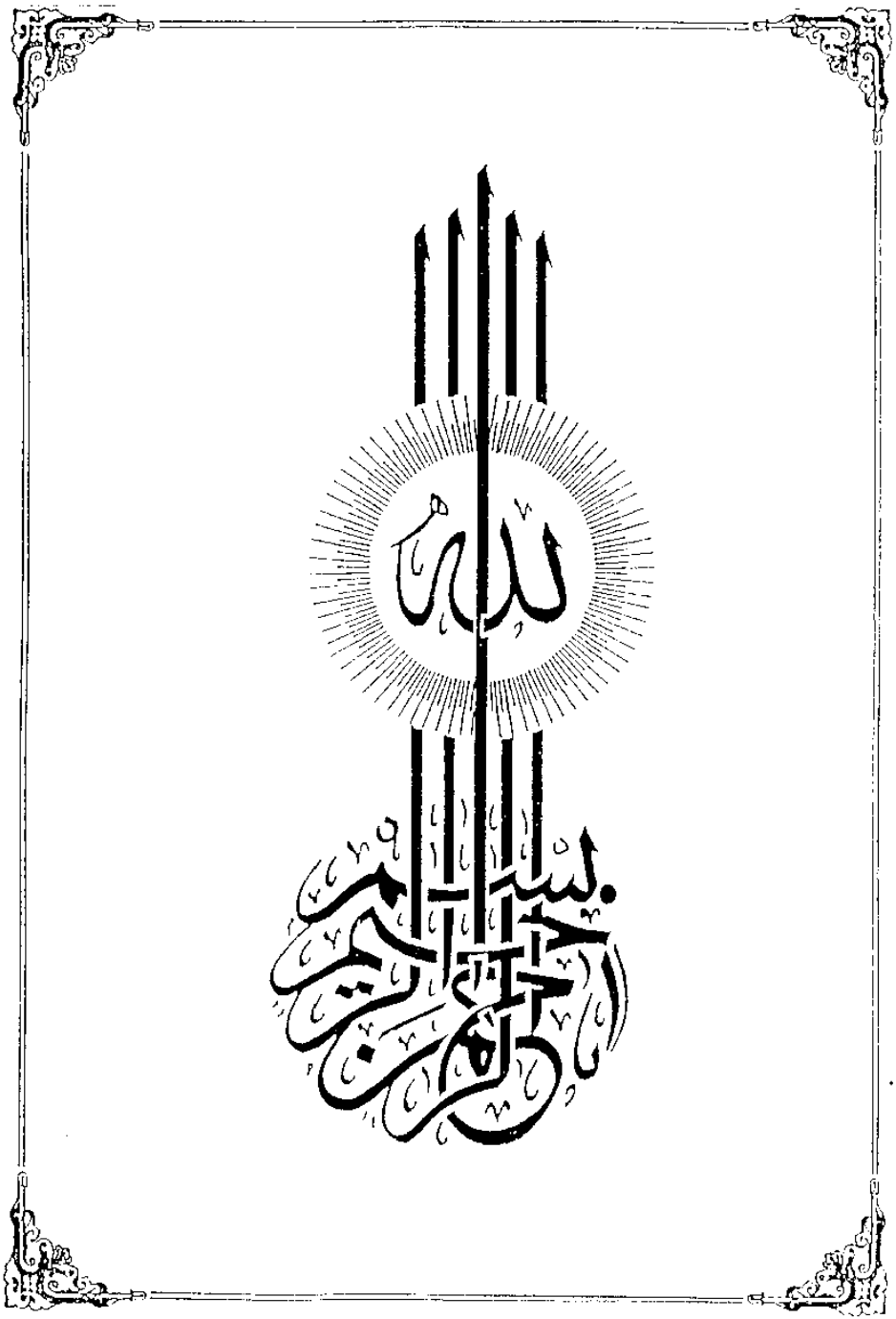

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INTRODUCTION

It is a well known fact that insulin secretion is disturbed in cases of juvenile onset diabetes (Felber et al., 1976). In the other hand, in cases of adult onset diabetes, the picture is less clear. Controversial reports were given by different authors. Some showed decreased levels of insulin in cases of diabetes (Billing et al., 1966), while others reported decreased insulin in impaired glucose tolerance (Ooi et al., 1965). On the other hand, others showed increased insulin levels in impaired glucose tolerance and early diabetes (Hoffman et al., 1966).

AIM OF WORK

In this present work, we aim to study the level of insulin in cases of adult onset diabetes and to assess the relation of the insulin level to the duration of diabetes.

REVIEW OF LITERATURE

[I] DIABETES MELLITUS

DEFINITION :

Diabetes mellitus is one of the very important endocrinal disorders. It comes second to obesity in its prevalence. Its degree of extent is difficult to be assessed, because of the imperfect distinction between normal and diabetic, particularly in old people (George and Cahill, 1985).

It is not a single disease entity, but, it can be defined as a syndrome involving a variety of metabolic problems. The prominent features of this syndrome are most probably relevent to an absolute or relative deficiency, or inefficiency of insulin and its functions. It seems to have amongst other factors, certain hereditary rooting. It is also associated with accelerated atherosclerosis and predisposes to certain specific microvascular abnormalities including retinopathy, nephropathy and neuropathy. There are also other associated problems, such as the lowering of resistance towards infection, especially if the diabetes is poorly controlled (George and Cahill, 1985).

CLASSIFICATION :

Recently, the results of both clinical and laboratory studies have demonstrated that the complex condition of D.M. is heterogeneous in cause and type (Pajans et al., 1976). Over the years, this has led to a consideration of classification by groups of knowledgeable workers with a goal of developing an international agreement as to diagnostic procedures, criteria and terminology. This classification was introduced by the European Society for the Study of Diabetes (E.S.S.D.) and was also agreed upon by the National Diabetes Data Group (N.D.D.G.) of the National Institute of Health, 1979.

Clinical types of D.M. :

Type I : Insulin-dependent D.M. (I.D.D.M).

Type II: Non-insulin-dependent D.M. (N.I.D D.M).

Type I (I.D.D.M) :

Patients with this type have a relatively abrupt onset of classic symptoms. The level of insulin is usually decreased and it may become totally absent after months or years. This type usually has an aggressive character with proneness to develop ketoacidosis. Patients usually depend on exogenous insulin for maintenance of health and normal life style. The onset is usually in childhood,

adolescence or young adulthood, but it may occur later in life (Marble and Ferguson, 1985).

Autoimmunity may play a role in its pathogenesis. Certain histocompatibility antigens (HLA) on chromosome 6 may be present (HLA B_{15} B_{18} B_{35} , DW_3 and DW_4) (Marble and Ferguson, 1985). This type of D.M. appears to be heterogeneous as to hereditary and environmetnal factors. Viral infections have been incriminated, but not conclusively proved to be a cause (Stiller et al., 1983).

Type II (N.I.D.D.M) :

This type often has an insidious onset with few or no classic symptoms of diabetes. In contrast to type I, patients of this type are not dependent on exogenous insulin for survival. Although the vast majority of patients develop the disease after the age 45, it may occur in adolescence or young adult life (Tattersall and Pyjans, 1975).

Plasma insulin levels may be normal, slightly or moderately below normal or even increased in early stages (Marble and Ferguson, 1985). Patients with N.I.D.D.M. may be divided to those who are obese or non obese. The majority are obese. Hyperglycaemia and glucose tolerance are improved by loss of weight and maintenance at the

lower level attained (Sopko et al., 1985). No characteristic pattern of HLA types has been noted. Islet cell antibodies have not been demonstrated (Tattersall and Fajans, 1975). Studies on identical twins indicate the strong influence of heredity (Tattersall and Pyke, 1972).

Pathogenesis of D.M. :

As I.D.D.M. and N.I.D.D.M. differ both in clinical presentation and presumed aetiology, a precise understanding of the pathogenesis of each type is essential. Although it is true that hyperglycaemia is a common factor shared by both types, yet their pathogenesis are different (Flier and Roth, 1978).

Type I diabetes is clearly associated with an absolute defficiency of insulin secretion. The insulin defficiency is easily demonstrable, when we measure circulating insulin level in either the basal or stimulated state. Insulin defficiency is present at the time of onset of the disease and throughout the entire clinical course. Some residual B-cell function may be seen as demonstrated by C-peptide measurements. Transient periods of remission can occur producing the so-called honeymoon phase of the disease (Rubenstein et al., 1977).

The lack of insulin secretion in type I D.M. appears to result from an autoimmune process involving probably the pancreatic insulin-producing beta cells, leading ultimately to their destruction with the development of the syndrome (Kahn, 1985). This autoimmune process is probably triggered by some environmental factors in a genetically susceptible individual. The nature of such factors, however, is so far unknown , yet experimental studies suggest a possible viral or toxic involvement (Grunfeld et al., 1985).

Type II D.M. is by far the more common form of the disease, but its pathogenesis remains even less clear and more controversial than that of type I. This type is not associated with any specific HLA alloantigens, but is clearly genetically influenced since it occurs in identical twins with almost total concordance (Barnett et al., 1981).

Type II D.M. is associated with obesity in more than 80% of cases, suggesting the possibility that this type of D.M. may be due to a disordered mechanism of appetite regulation or energy expenditure. The effects of obesity may be partially explained by the fact that muscle cells enlarge , thereby reducing the access of insulin to its

site of action. This leads to insulin resistance and hyperglycaemia (Lillioja et al., 1987).

In contrast to the patients with type I, type II diabetics have considerable preservation of the beta cell mass (Holman and Turner, 1979). They often secrete substantial quantities of insulin into the circulation. This has led to the idea that, in type II diabetes there is resistance of the peripheral tissues to respond to insulin (Kolterman et al., 1981). There is still considerable controversy as to which of these factors : decrease insulin secretion or insulin resistance, is the major or primary one in the pathogenesis of type II D.M. It seems likely that there is an interplay of both, leading to the final disease manifestations (Weir, 1982).

It is not known what causes beta cell secretory deficiency in cases of NIDDM. Glucose itself can have adverse effects on the pancreas. Beta cells of all persons are susceptible to this glucose toxicity. However, only those with some intrinsic abnormality of beta cells become unresponsive and thus diabetic (Unger and grundy, 1985).

Persons with NIDDM lack regular oscillatory insulin secretion (Lang et al., 1981) and thus have less tightly