# RENAL THRESHOLD VARIATION AMONG DIFFERENT TYPES OF DIABETES MELLITUS

THESIS

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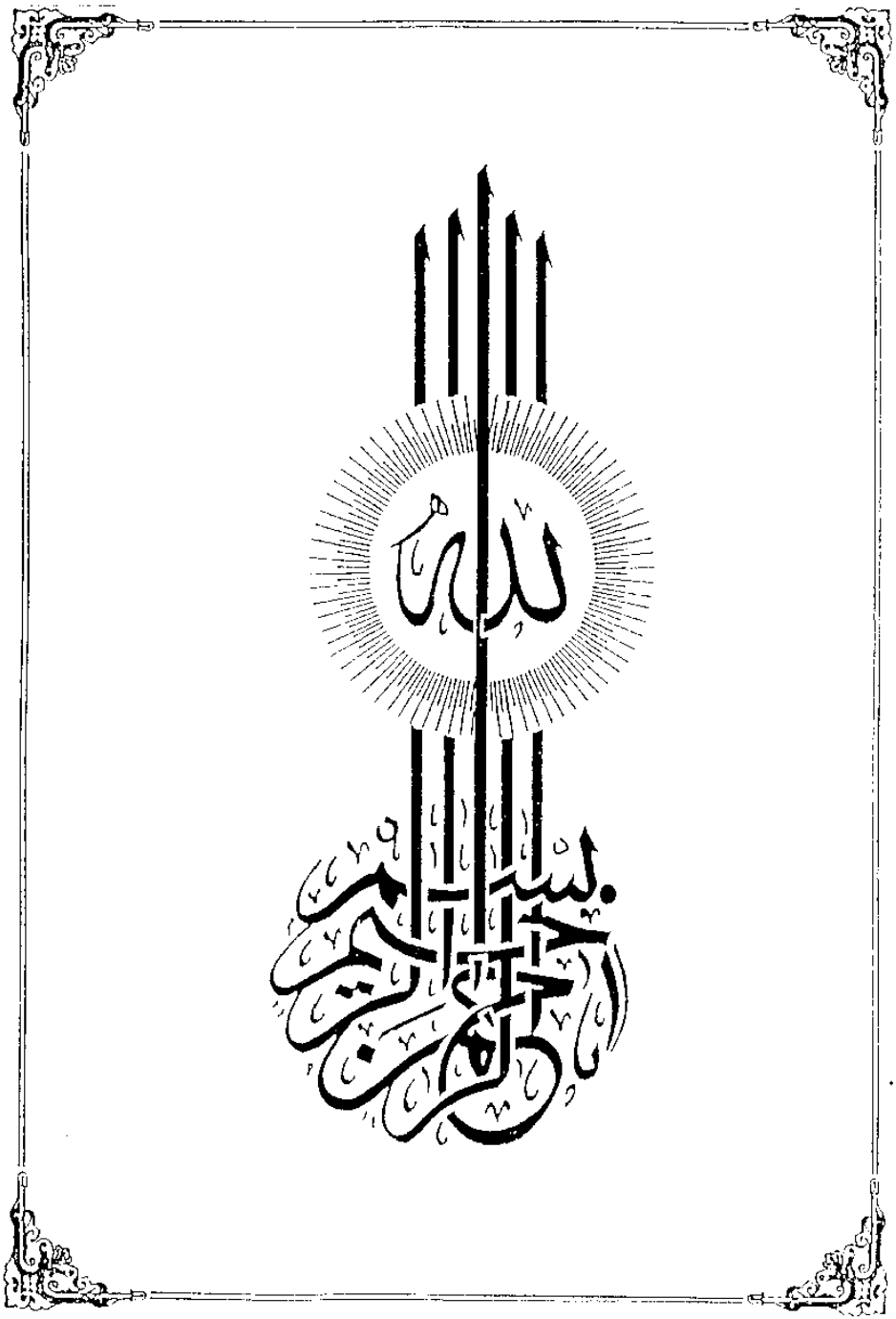

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# INTRODUCTION
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## INTRODUCTION and AIM of work

It is a well known clinical fact that the amount of glucose in the urine of a diabetic does not always faithfully reflect his blood sugar level, some diabetic patients may have hyperglycemia without glucoseuria or the reverse.

The aim of this work is to try to find out factors influencing the renal threshold in diabetes and the relation between blood and urine glucose both in type I,type II, and also in control subjects by injection of 5% dextrose by I.V drip and collecting a blood and urine sample every 20 min for 120 min, and also probably finding a rule or guide to the clinician as to which type of case he expects the urine glucose to be reliable or otherwise in managing a case of diabetes.

Glucoseuria in diabetes is secondary to hyperglycemia but its extent may give a misleading impression of the height of the blood glucose.

Glucoseuria occurs when the load of glucose in the glomerular flow exceeds the maximal rate of glucose reabsorbtion in the tubules ( Tmg). The load depends on the concentration of glucose in plasma, the glomerular filtration rate (GFR0) and the tubular reabsorbtion.

A fixed renal threshold therefore is only possible when these factors are constant and in fact, they are in most normal subjects. The osmotic diuresis provoked by glucoseuria produced may be the characteristic feature of diabetes mellitus i.e. excretion of water, sodium and potassium resulting in polyuria, polydepsia and lassitude. In diabetic ketosis the loss of salt and water result in contraction of the extracellular fluid space and blood volume. thus in turn, result in renal vaso constriction,diminished renal blood flow and glomerular filteration. Diminished G.F.R. may reach a low level that all ketone bodies and glucose are reabsorbed and non appear in the urine. Potassium deficiency also aggravates the fall in glomerular filteration rate (G.F.R.0) (walker etal., 1984).

# REVIEW OF LITERATURE

# DIABETES MELLITUS

## DEFINITION:

Diabetes Mellitus is one of the common metabolic disorders of humans. (Foster 1980)

The word diabetes derives from the greek meaning siphon. (Hostetter 1986).

It may be defined as a metabolic disorder in which chronic hyperglycemia with or without glucoseuria is the essential feature (Drury 1986).

## CLASSIFICATION:

Diabetes mellitus could no longer be considered as a single disease entity (Alford 1986). We should really think of DM as the diabetic syndrome (Drury 1986). Previously, several attempts had been made to classify diabetes according to age of onset, insulin requirements, degree of glucose intolerance and prediposition to develop ketosis. The most logical classification of the diabetic syndrome would be based on knowledge of it's pathogenesis but in most instances this is not known, thus, no classification is completely satisfactory (Bennett 1983).

The classification recommended by the **NATIONAL DIABETES DATA GROUP** and subsequently adopted by **WHO EXPERT COMMITTEE ON DIABETES** is:

1) Insulin-dependent ketosis-prone type of DM (type -1 diabetes).
2) Non-insulin dependent non ketosis-prone type (type -2 diabetes).
3) Diabetes associated with certain conditions and syndromes e.g. pancreatic diseases, hormonal imbalance, certain genetic syndromes, drugs and chemicals.
4) gestational diabetes which is restricted to women who develop glucose intolerance during pregnancy.
5) Impaired glucose tolerance which is a term restricted to individuals, their plasma glucose levels between normal and those considered diabetic.
6) Individuals with normal glucose tolerance who have experienced transient hyperglycemia be classed as " previous abnormality of glucose tolerance ".
7) individuals who are at high risk to develop DM,, be classed as potential abnormality of glucose tolerance. (National diabetes data group 1979, Bennett 1983, Welborn 1984, Drury 1986).

**DIAGNOSIS**:

Diagnosis of symptomatic diabetes is not difficult, a patient presents with polyuria, polydpisia, weight loss,

fatigue and is found to have hyperglycemia (Foster 1980). However, many patients are asymptomatic and only come under suspicion when glucoseuria is noted on routine examination (Drury 1986).

The diagnosis of diabetes may be established solely on the bases of fasting venous plasma glucose concentration when the level of which is greater than 7.8 mmol/L (140 mg/dl) on more than one occasion (National diabetes data group 1979).

In certain situations when a considerable doubt exists about patient glucose tolerance, fasting level is less than 140 mg/dl, these cases exhibit sustained elevated venous plasma glucose values during an oral glucose tolerance test using 75 gm oral carbohydrate load (National diabetes data group 1979). Values > 200 mg/dl at 2 hr. after ingestion of carbohydrate dose and also at some other time point between time 0 and 2 hr., are diagnostic (Bennett 1983, Welborn 1984, Heine 1985, Drury 1986).

With strict application of above criteria, there will be a group of patients in whom the values, whilst not diagnostic of DM, lie outside the normal range, this is the group of impaired glucose tolerance (IGT) (Drury 1986)>

The WHO criteria for diagnosis of IGT specify that the fasting blood glucose should be normal and the 2 h. blood glucose is greater than 140 mg% but less than 200 mg% (Heine 1985, Drury 1986).

Specific criteria for diagnosis of Gestational DM, based on the study of O'Sullivan and Mahan in 1964, have been adopted by national diabetes data group (NDDG 1979).

An oral glucose tolerance test is performed over 3 hr. using 100 gm oral glucose load with sampling at zero, 1, 2, 3, hours. The test is abnormal when any two of the following values are equaled or exceeded .

| | |
|---|---|
| Fasting venous plasma glucose value | 105 mg% |
| 1-h value | 189 mg% |
| 2-h value | 165 mg% |
| 3-h value | 146 mg% (Drury 1986) |

## AETIOLOGY AND PATHOGENESIS:

### Type 1 DIABETES:

The prime aetiological factor in IDD is absolute or near absolute insulin deficiency (Andereani 1984). This insulin deficiency results from corresponding degrees of b-

cell malfunction (Drury 1986). 90% of the b-cell mass has to be destroyed before chronic hyberglycemia develops (Drury 1986).

The cuses of b-cell mass distruction is unknown (Doniach 1983). It is possiple that a genetic susceptibility interacts with inviromental agents and immunological factors producing the typical clinical syndrome (Andereani 1984).

1) GENETIC FACTORS:

Studies of the HLA antigens have provided new evidence for the existance of heterogenity in diabetes (Pyke 1979). There is clear evidence of an association between certain HLA antigens and IDD with increased relative risk when possessing certain HLA-A and HLA-B antigens (Cudworth 1978)). The strongest association with the desease lie with the DR antigens, HLA-DR3 (Sachs et al., 1980) , and HLA-DR4 (Deschamps et al., 1980).

58% of IDD patients were found to be DR3 positive and 42% DR4 positive, this suggests that the diabetogenic genes may be closer to the HLD-d locus than the HLA-A, B, C loci (Cudworth 1978).

Several studies have shown in siblings of IDDs, a statistically significant association between the

sharing of identical haplotypes and the develpment of IDD, this could support the existance of HLA linked predispoing genes (Barbosa 1977).

In identical twins, the concordance for DM when age of onset is less than 45 y. is about 500% in contrast with the concordance of about 100% when age of onset is greater than 45 y. (Pyke 1979, Barnett 1981). Current evidence supports the possibility of two diabetogenic genes on the 6th chromosome in linkage disequilibrium with either DR3 or DR4 (Nelson 1975). It is not clear yet wheather it is the DR antigens themseves which confer susceptibility to DM or they are juxtaposed with diabetogenic genes which have not yet been isolated (Drury 1986).

2) Immunological Factors:

Several studies has been made to show the role of immunological factors in the pathogenesis of IDD based on the observation that IDD may be associated with other autoimmune endocrinopathies (Nnerup et al., 1971).

In 1974, islest cell antibodies were described in some diabetics with otherautoimmune disorder (MacCuish et al., 1974). These antibodies are found in a high percentage of IDDs and apear to have a close relationship in time with B-cell damage (Irvine 1977).

Other antibodies that are found to react the surface