# PROSTAGLANDINS IN DIABETES MELLITUS

THESIS

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General Medicine

by

Mohamed Khaled M . A . Khalil

M.B., B.Ch.

supervisors

Prof.Dr

HUSSEIN EL SAYED M. EL-DAMASY

Professor of Medicine

Prof.Dr

SAYED M. RAFFAT

Professor of Medicine

Dr.

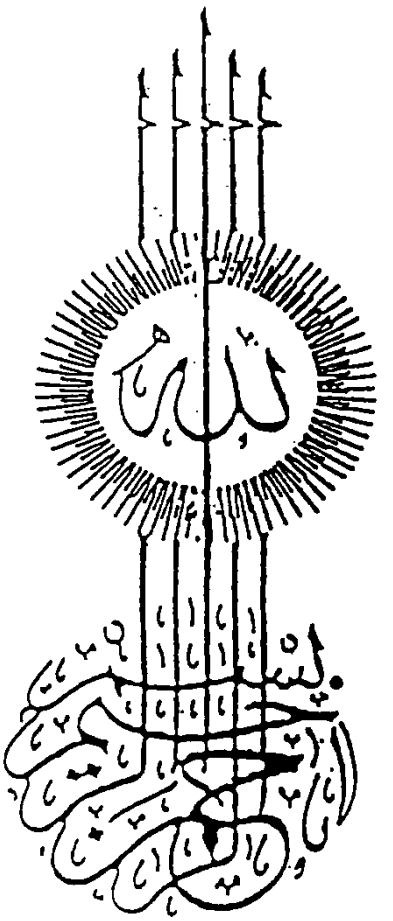
Sohair Gamal El Din

Lecturer of Medicine

Faculty of Medicine

Ain Shams University

Cairo- Egypt



الحمد لله الذى هدانا لهذا وما كنا لنهتـــــدى

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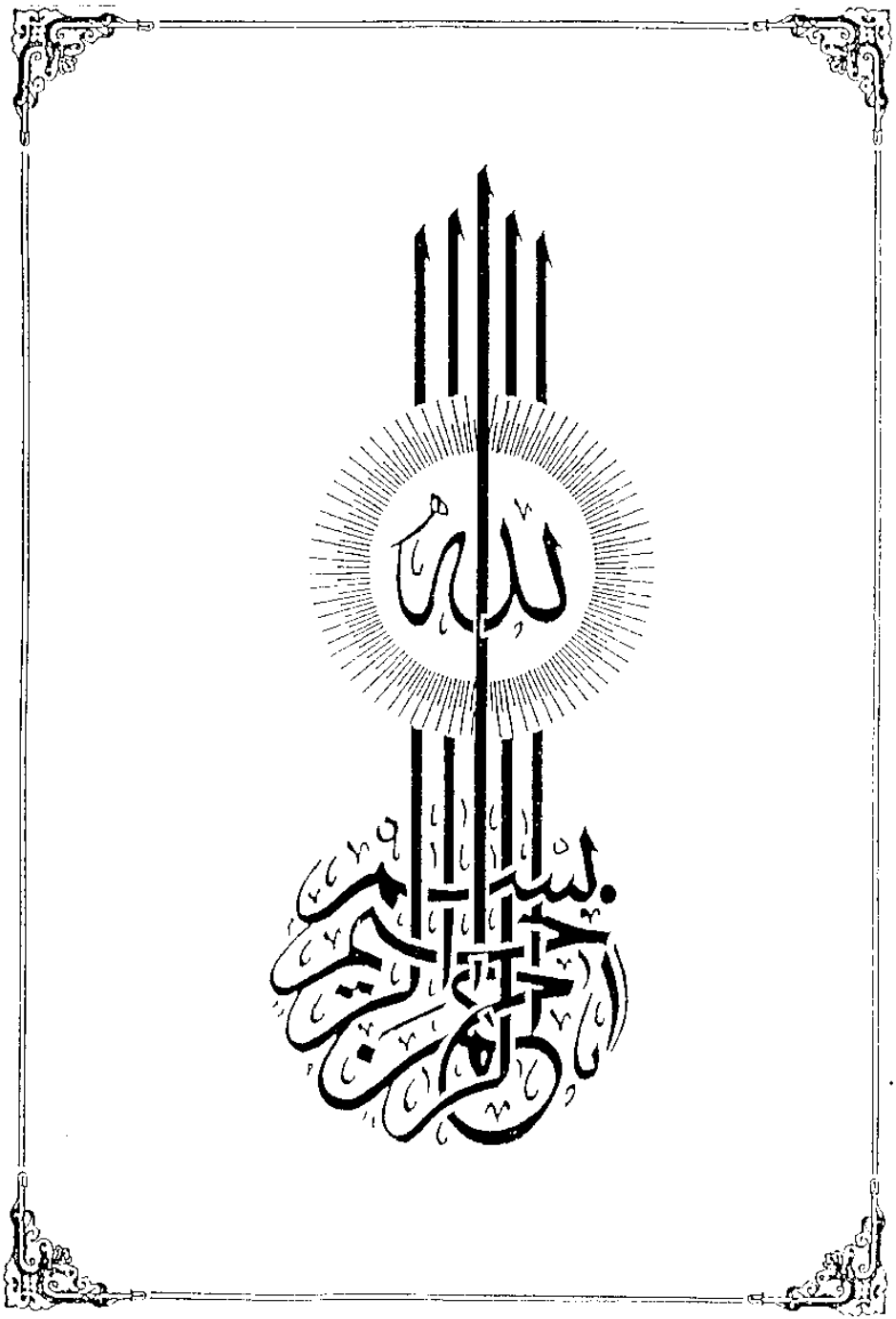
صدق الله العظيم



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## Abbreviations

- ACTH : Adrenocortico trophic hormone
- ADH : Anti diuretic hormone
- AODM : Adult onset diabetes mellitus
- ATP : adenosine triphosphate
- cyclic AMP : cyclic 3,5 adenosine monophosphate
- cyclic GMP : cyclic 3,5 guanosine monophosphate
- DNA : Deoxyribo nucleic acid
- GH : Growth Hormone
- HDL : high density lipoprotein
- HLA : histocompatibility leucocytic antigens
- IDDM : insulin dependent diabetes mellitus
- JODM : juvenile onset diabetes mellitus
- LH : Lutenizing Hormone
- ng. : nanogram
- NIDDM : Non insulin dependent diabetes mellitus
- NSAID : Non steroidal anti-infammatory drugs
- PGS : Prostaglandins
- $PGI_2$ : Prostacyclin
- pg. : picogram
- RCS : rapid contracting substances
- RNA : Ribo-nucleic acid
- $T_3$ : Tri-iodo thyronine
- $T_4$ : Tetra-iodo thyronine ( Thyroxine)
- $TXA_2$ : Thromboxanes
- VLDL : very low density lipoprotein

# INTRODUCTION

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# AIM OF THE WORK

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The role of prostaglandins in diabetes mellitus and its effect on glucose homeostasis and blood lipids has been a point of interest to study.

Many investigators demonstrated the effects of prostaglandin E on beta cell function. PGE was observed to stimulate insulin secretion both in vivo (Bressler et al , 1968) and in vitro (Johonson et al.,1973).

On alpha cells, the role of prostaglandin E is controversal. Sacca and Perz (1976), reported that prostaglandin $E_1$ infusion stimulate glucagon secretion. While Giugliano et al (1979), reported glucagon sec-secretion during $PGE_1$ infusion in man.

The aim of this work is to study the changes of PGE in normal and diabetics, with comparison to the blood glucose and total lipids.

# DIABETES MELLITUS

## Definition :

Diabetes Mellitus is a syndrome best characterised as a state of chronic hyperglycaemia with various aetiologies. It may present with acute symptoms that include thirst, polyuria, unexplained weight loss and these can progress to life threatening ketoacidosis or hyperosmolar coma. Subacute symptoms include the above together with pruritis valvae, balanitis, other skin infections, unusual fatigue or visual impairment . Chronic hyperglycaemia may be asymptomatic but is generally recognized as a predisposing risk factor for specific microvascular complications, namely retinopathy and nephropathy. ( Welborn T.A., 1980).

## Classification Of Diabetes :

In the development of concept of diabetes, it is necessary to recognize its various types. The practical classification is devided into :

(1) Primary idiopathic diabetes with insulin- dependent and non insulin- dependent diabetes.
(2) Secondary diabetes in which abnormalities in glucose handling may be caused by pancreatic disease, other endocrine diseases such as adrenocortical hormone excess and acromegaly, drug induced abnormalities, and chromosomal and genetic syndromes. ( Edward J. Busick., 1982).

Our study is concerned with the primary types of diabetes mellitus .

(A) Insulin Dependent Diabetes Mellitus
( IDDM, JODM, TYPEI)

This type of diabetes is aggressive both in its begening and course. Several markers are recognized to characterize this group of patients. The most important is relation to diabetic family. In the predisposed person, the environmental factors such as viral infections may trigger the disorder, or an autoimmune response directed against the beta cells may lead to rapid development of diabetes.
Typically, the onset is abrupt with polyuria and polydipsia. This is rapidly progress to ketoacidosis.

Insulin is needed from the onset. On insulin, glucose values become stabilized. These patients loose if not all their ability to produce endogenous insulin.

(B) Non Insulin Dependent Diabetes Mellitus :
( NIDDM, TYPE II)

The principal features of this type are onset in middle aged and eldery patients, absence of ketoacidosis, and control of blood sugar levels with carbohydrate restriction, weight reduction and use of oral hypoglycaemic agents. The most important factor influencing NIDDM is excessive caloric intake leading to obesity, changes in insulin receptors and change in the body response to endogenous insulin.

Their is no sharp or fixed dividing line between the two types of diabetes. The differance between the diabetes of childhood and that of adults however are vived enough to provoke that these two varieties truly represent the same disease.

Course Of Diabetes :

This classification is based upon the amount of carbohydrate intolerance and is classified into :

1- prediabetes :

It is present in the affected individual from conception and is latent until detectable carbohydrate intolerance develops. The time before development of abnormal glucose tolerance is referred as prediabetes or potential diabetes. It can be predicted only in the twin whose whomozygous sibling has already developed diabetes mellitus. Prediabetes can be suspected when both parents have diabetes or in women with certain characteristic obstetric or prenatal problems e.g. mothers who have babies that weight more than 4 kg. at birth or babies that have a high mortality rate in pregnancy or neonatal period.

2- Chemical Diabetes :

The changes from the prediabetic state to the detectable abnormal glucose tolerance is stable. . Initially the abnormal glucose tolerance is reversable,

and some patients can swing from one group to the other for sometime before becoming permanently diabetic. The fasting blood sugar level and the standard oral glucose test results may remain normal, and cortisone stimulation tion may be necessary to demonstrate carbohydrate intolerance. If the blood glucose level becomes high during cortisone stimulated glucose tolerance test, latent chemical diabetes is expected. It is present if the fasting blood glucose is still normal while the blood glucose in oral glucose tolerance test rises to higher than normal levels.

3- Overt Diabetes :

It exists when the fasting blood glucose is elevated and the glucose tolerance tests are abnormal. These patients usually have glycosuria and sometimes develop ketonuria.

## GLUCOSE HOMEOSTASIS

### Normal Blood Sugar Level :

Under normal conditions, the blood sugar level is fairly constant and varies within narrow limits. In the resting postabsorpative state the blood glucose concentration varies between 80-100 mg./ 100ml. After the ingestion of a carbohydrate meal it may rise to 120-130 mg./100ml. During fasting, the level falls to aroun 60-70 mg./100ml. (Harper et al., 1981).

This fasting level is maintained and not decreased below this level by two factors govern the metabolism of carbohydrate in the human body. Firstly, the brain and nervous tissue oxidize glucose only for energy purposes. Secondly the efficiency of the kidney in reabsorbing glucose from the glomerular filtrate.

If the fasting level decreased below 40-50 mg./100ml. the hypoglycaemic symptoms and signs will appear, and if the level decreased more, the subject will fall into coma. If the blood glucose exceeds the normal renal threshold (180 mg./100 ml.), the glucose appear in urine ( Harper et al., 1981).

## MECHANISMS REGULATING BLOOD GLUCOSE :

Blood glucose is kept constant at its normal levels as a result of a harmony between two opposing mechanisms. Firstly, sources of blood glucose and secondly the fate of blood glucose (Harper et al., 1981).

### Sources Of Blood Glucose :

1- From carbohydrates of the diet : most carbohydrates in diet are absorbed from intestine in the form of glucose, galactose and fructose. These are absorbed into portal circulation to the liver where galactose and fructose are converted to glucose.

2- Gluconeogenesis : this process includes formation of glucose from non carbohydrate sources either directly as glucogenic amino acids or indirectly which are products of partial metabolism of glucose in certain tissues and which are conved to the liver and kidney where they are resynthesized to glucose. Thus lactates formed by oxidation of glucose in skeletal muscles and erythrocytes are transported to liver and kidney where it forms glucose which again becomes available via circulation for oxidation in the tissues. This process is known as Cori cycle or lactic acid cycle ( Soling and Williams., 1971).