PLASMINOGEN ACTIVATOR INHIBITOR-1 (PAI-1) IN TYPE 2 DIABETIC PATIENTS

Thesis

Submitted For Partial Fulfilment
Of The Master Degree In Clinical And Chemical Pathology

By

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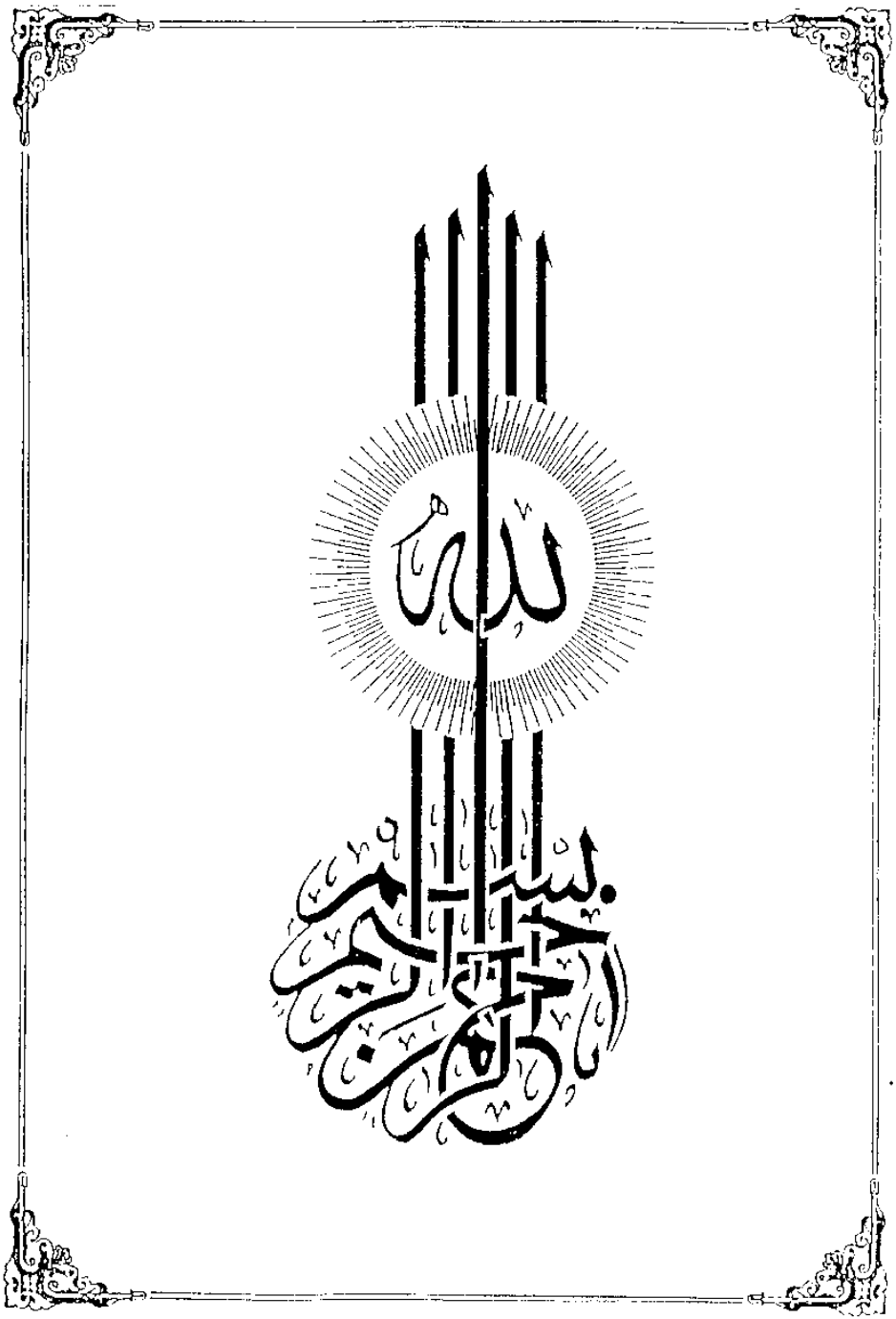
بسم الله الرحمن الرحيم

فالله خيرٌ حافظاً وهو أرحم الراحمين

صدق الله العظيم

سورة يوسف ٦٤



بسم الله الرحمن الرحيم

إقرأ باسم ربك الذي خلق

خلق الإنسان من علق

إقرأ وربك الأكرم الذي علم بالقلم

علم الإنسان ما لم يعلم

صدق الله العظيم

سورة العلق ١-٥

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LIST OF ABBREVIATIONS

ACAC:	Aceto acetic Acid
APS AC:	Acyl plasminogen streptokinase activator
D.M:	Diabetes mellitus
GDM:	Gestational diabetes mellitus
Hb:	Hemoglobin
HDL:	High density lipoprotein
HLA:	Human leucocyte antigen
HMG/Co	B-hydroxy-B-methyl glutaryl-coenzyme A
HMW UK:	High molecular weight urokinase
2 hrs P.P:	2 hours post prandial
IDDM:	Insulin dependent diabetes mellitus
IGT:	Impaired glucose tolerance
LMW UK:	Low molecular weight urokinase
NIDDM:	Non insulin dependent diabetes mellitus
OGTT:	Oral glucose tolerance test
OPD:	Ortho-phenylenediamine
PAIS:	Plasminogen activator inhibitors
PLG:	Plasminogen
Pot AGT:	Potential abnormality of glucose tolerance
Prev AGT:	Previous abnormality of glucose tolerance
SDS:	Sodium dodecyl sulphate
SK:	Streptokinase
T.G:	Triglyceride
t-PA:	Tissue plasminogen activator
UK:	Urokinase
U-PA:	Urokinase-like plasminogen activator.

INTRODUCTION & AIM OF THE WORK

INTRODUCTION

A variety of abnormalities of the hemostatic system have been reported in diabetic patients. Since most of these abnormalities indicate a hypercoagulable and hypofibrinolytic state leading to enhanced intravascular fibrin deposition, they have been linked to the high incidence for cardiovascular morbidity and mortality among these patients (**Juhan-Vague et al., 1991**).

Fibrinolytic activity has been reported to be normal, elevated or low in diabetic patients (**Ostermann and Vandeloo, 1986**). This activity is mainly dependent on the plasma levels of tissue plasminogen activator (t-PA) and plasminogen activator inhibitors (PAIS) usually PAI-1. A hypofibrinolytic state, therefore, may result from decrease of t-PA or increase of PAI-1 or both. In type 2-diabetic patients, increased levels of PAI-1 have been described (**Auwerx et al., 1988 and Juhan-Vague et al., 1991**). The increase of PAI-1 was found to be correlated to the degree of obesity and parameters of lipid metabolism (**Juhan-Vague et al., 1989**). In another study, by contrast, neither t-PA nor PAI-1 was significantly increased in type 2- diabetics compared with the controls.

AIM OF WORK:

This work aimed to investigate the effect of diabetes and metabolic effects on the plasma levels of PAI-1.

REVIEW OF THE LITERATURE

FIBRINOLYTIC SYSTEM

I. FIBRINOLYTIC SYSTEM

A) DEFINITION:

Fibrin formation is a central feature of inflammation, tissue repair, and hemostasis. These reactions are temporary and their effects are curtailed or reversed in order to restore normal tissue structure and function when the inciting stimulus is removed. Thus, a fibrin clot which forms quickly in a torn blood vessel to stem the loss of blood is remodeled and removed to restore blood flow. The principal effector of clot removal is the fibrinolytic system, which controls the enzymatic degradation of fibrin (**Williams et al., 1993**).

The coordinated action of activators, zymogens, enzymes and inhibitors provides for local reaction at sites of fibrin accumulation without systemic effects.

In the blood, fibrinolysis results from the conversion of an inert plasma proenzyme (Plasminogen) into a proteolytic enzyme (plasmin), the main physiologic role of which presumably is the proteolytic dissolution of fibrin.