CORRELATION BETWEEN FACTOR VIII CLOT-PROMOTING FUNCTION AND MICROVASCULAR DIABETIC RETINOPATHY

THESIS

SUBMITTED FOR THE PARTIAL FULFILMENT OF
THE MASTER DEGREE OF
INTERNAL MEDICINE

BY

ANWAR AHMED ESMAIL
M. B., B.CH

SUPERVISED BY

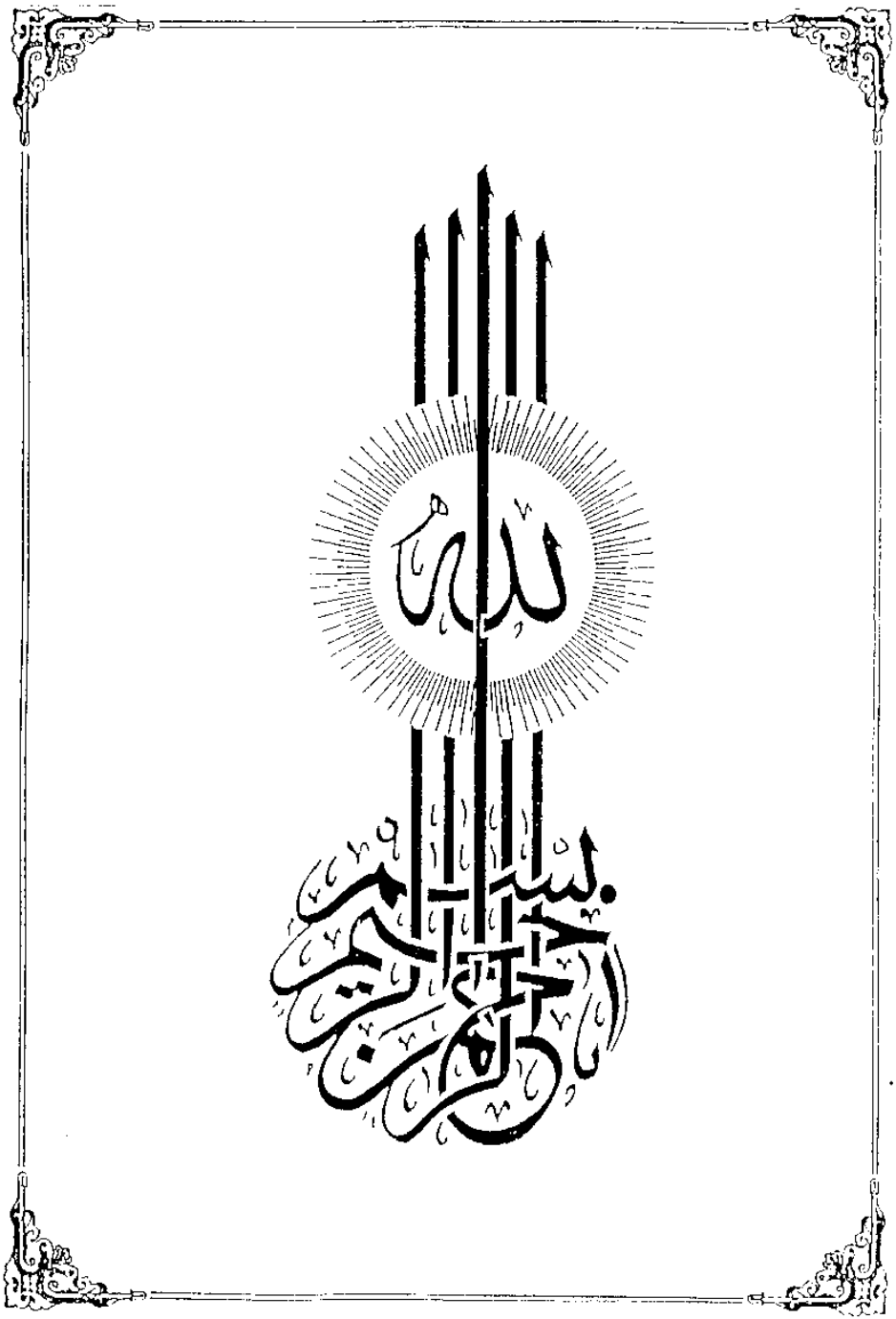
PROF. DR. SAAD ABDUL MAGEED FARRAG
PROFESSOR OF INTERNAL MEDICINE
AIN SHAMS UNIVERSITY

PROF DR. M. REFAAT GABALLA
ASSISTANT PROFESSOR-CLINICAL PATHOLOGY
AIN SHAMS UNIVERSITY

COSUPERVISOR DR. ALAA ALI ABDUL RAHMAN
LECTURER OF INTERNAL MEDICINE

1987

Acknowledgement



ACKNOWLEDGEMENT

I wish to express my gratitude to Dr. SAAD ABDUL MAGEED, Prof. of Internal Medicine, Faculty of Medicine, Ain Shams University, under whose guidance and constant supervision this thesis has been prepared.

To Dr. REFAAT GABALLA, assistant Prof. of Clinical Pathology, Faculty of Medicine, Ain Shams University, I owe a great deal, since he was generous with his time, his efforts and his valuable suggestion without which this thesis would not have taken its present form.

I am deeply touched with the great efforts of Dr. SOHEER GAMAL EL-DIN, Assistant Professor of Internal Medicine, Faculty of Medicine, Ain Shams University, who revised this work several times with patience.

I'm also deeply indebted to Dr. ALAA ABDUL RAHMAN, Lecturer of Internal Medicine, Faculty of Medicine, Ain Shams Univesity, for his great efforts, continious encouragement, and sincere help throughout the whole work sparing no effort in helping me in every step in this thesis .

Despite this wealth of assistance, any inaccuracy or shortcoming, is still my responsibility.

ABBREVIATIONS

ADP	= Adenosine Disphosphate
ATIII	= Antithrombin III
BL.P	= Blood Pressure
2,3 DPG	= 2,3 Diphosphoglycerate
F	= Female
F. H	= Family History
F. VIII:C	= Factor VIII Coagulant Activity
F. VIII-C	= Factor VIII Coagulant Protein
F. VIII:Ag	= Factor VIII Coagulant antigen
F. VIII C:Ag	= Factor VIII Coagulant antigen
F. VIII C/Ag	= Factor VIII Coagulant antigen
F. VIII-agn	= Factor VIII Coagulant antigen
F. VIII R:Ag	= Factor VIII Related Antigen
F. VIII:Rco	= Factor VIII Related Cofactor
F. VIIIR:Rco	= Factor VIII Related Ristocetin Cofactor
vWF	= von Willebrand Factor
G. H	= Growth Hormone
HbA	= Haemoglobin A
IDDM	= Insulin Dependent Diabetes Mellitus
LDL	= Low Density Lipoprotein
M	= Male
NIDDM	= Non Insulin Dependent Diabetes Mellitus
PF4	= Platelet Factor 4
PGI2	= Prostacyclin
RER	= Rough Endoplasmic Reticulum
SEM	= Standard Error of the Mean
R.B.S.	= Random Blood Sugar
TXA2	= Thromboxan A2

CONTENTS

LIST OF TABLES OF THE RESULTS

LIST OF ILLUSTRATIVE DIAGRAMS

Introduction & Aim of the Study

INTRODUCTION

In patients with diabetes mellitus, the rates of morbidity and mortality are strikingly increased as result of both macro- and micro-vascular disease. Recent evidence suggests involvement of the haemostatic system in the initiation or propagation of vascular lesion. (Jones and Peterson , 1983)

Microvascular disease is one of the dreadful complications of diabetes mellitus. Microvascular complication in diabetes seems to be multifactorial in origin and recently, microvascular diseases were found to be associated with Hyper Coagulable State (Reavan and Steiner, 1981)

Many reports are available regarding the concentrations of various coagulation Factors in diabetic patients. High level of Factor VIII is most frequently reported in diabetic patients (Gensini et al, 1979) but the correlation between elevated Factor VIII and diabetic Microvascular disease is not well studied in Literature.

AIM OF THE WORK

TO SEARCH FOR A RELATION BETWEEN FACTOR VIII-CLOT PROMOTING ACTIVITY AND MICROVASCULAR DISEASE IN THE FORM OF DIABETIC RETINOPATHY.

Review of Literature

CHAPTER I

VASCULOPATHY AND THROMBOTIC COMPLICATIONS IN DIABETES MELLITUS

The prevalence of diabetes throughout the world has been established from 1.5% to 5% of the world population. There is a true variation in the prevalence of diabetes among different racial and ethnic groups and other factors influence the prevalence of diabetes within a society including the age, sex, familial characteristics, dietary habits and obesity.

Even if exact prevalence cannot be ascertained, diabetes remains a significant cause of suffering in all countries among all races. It has been estimated that over the past decades, diabetes has killed more than all the wars put together. (L' Esperance, 1981).

Definition:

Diabetes is a diagnostic term applied to constellation of anatomic and bio-chemical abnormalities which share in common, as part of a syndrome, a disturbance in Glucose Homeostasis, which is secondary to a deficiency in the beta cells of the endocrine pancreas.

This bulky and vague definition cannot be made more specific, owing to the marked variability in the disorder (Camerini et al , 1979).

FAJAN in 1977, used the term "IdiOpathic Diabetes Mellitus" in which an inherited susceptibility play an important role.

The susceptibility has its origin at Conception and may exist for prolonged periods before an additional pathogenic factors of environmental origin cause the emergence of recognizable abnormality of carbohydrate metabolism.

Thus a definition of genetic or idiopathic diabetes mellitus should include stages in the natural history of the disease which presently cannot be recognized since we lack a marker for "genetic diabetes" (Rotter and Rimion, 1981).

Haematologic Abnormalities Associated with Diabetes:

White Blood Cells:

Numerous functional abnormalities have been demonstrated including defective granulocytic adherence, chemotaxis, phagocytosis and intracellular bactericidal activity (Bagdade et al, 1978 and Nolan et al, 1978). Also there is deminished proliferative responses to mitogen stimulation and decrease in T and B-cell surface membrane markers(Selam et al, 1979).

Although the clinical significance and revelance to micro-angiopathy of these abnormalities in leukocyte cell surface are unclear at present, similar alteration in the surfaces of the other cells from diabetic persons could have important implications.

Still, all of these impairments can be reversed by tighter diabetic control(Edelman, 1976).

Red Blood Cells:

It has been argued that increased aggregation of red blood cells , which has been obseved in the blood of diabetic patients, may contribute to obliterative microvascular changes in the retina (Little et al , 1977), together with decreased red cell deformability which might seriously hamper rapid and homogenous perfusion within the microcirculation(Mc Millan et al, 1978).

Baba et al, 1979 and Miller et al, 1980, have been attributed the reduced red cell deformability to the higher degree of erythrocyte membrane microviscocity which may perhaps be due to glycosylation of membrane proteins. Patients with inadequately controlled diabetes may exhibit two to three folds elevation in three of the minor haemoglobin: Hb A1a, Hb A1b, Hb A1c thereby reflecting the degree of hyperglycemia (Trivelli et al, 1971, and Mc Donald et al, 1978), as the rate of formation of glycohaemoglobin is proportional to the integrated concentation of blood glucose. (Stevens et al, 1977, and Bennette al, 1978). In comparison to Hb A1o, Hb A1a has lower O2 affinity, whereas Hb A1b and Hb A1c have higher O2 affinity (Mc Donald et al, 1979).

In diabetes, the combination of relative deficiency of 2,3 DPG and elevated glycohaemoglobin levels during periods of change in blood glucose level may result in decreased oxygen delivery to critical tissues i.e