PLASMA THROMBOMODULIN; A NEW MARKER OF DIABETIC MICROANGIOPATHY

Thesis
Submitted for partial fulfillment of
M.S Degree in Clinical and Chemical Pathology

By
Amaal Abdel Hamid Mohammed
(M.B., B.Ch.)

Under the supervision of
Prof. Dr. Fadila Hassan Sabry
Professor of Clinical Pathology
Faculty of Medicine, Ain Shams University

Dr. Ibrahim Youssef Abdel Messih
Lecturer in Clinical Pathology
Faculty of Medicine, Ain Shams University

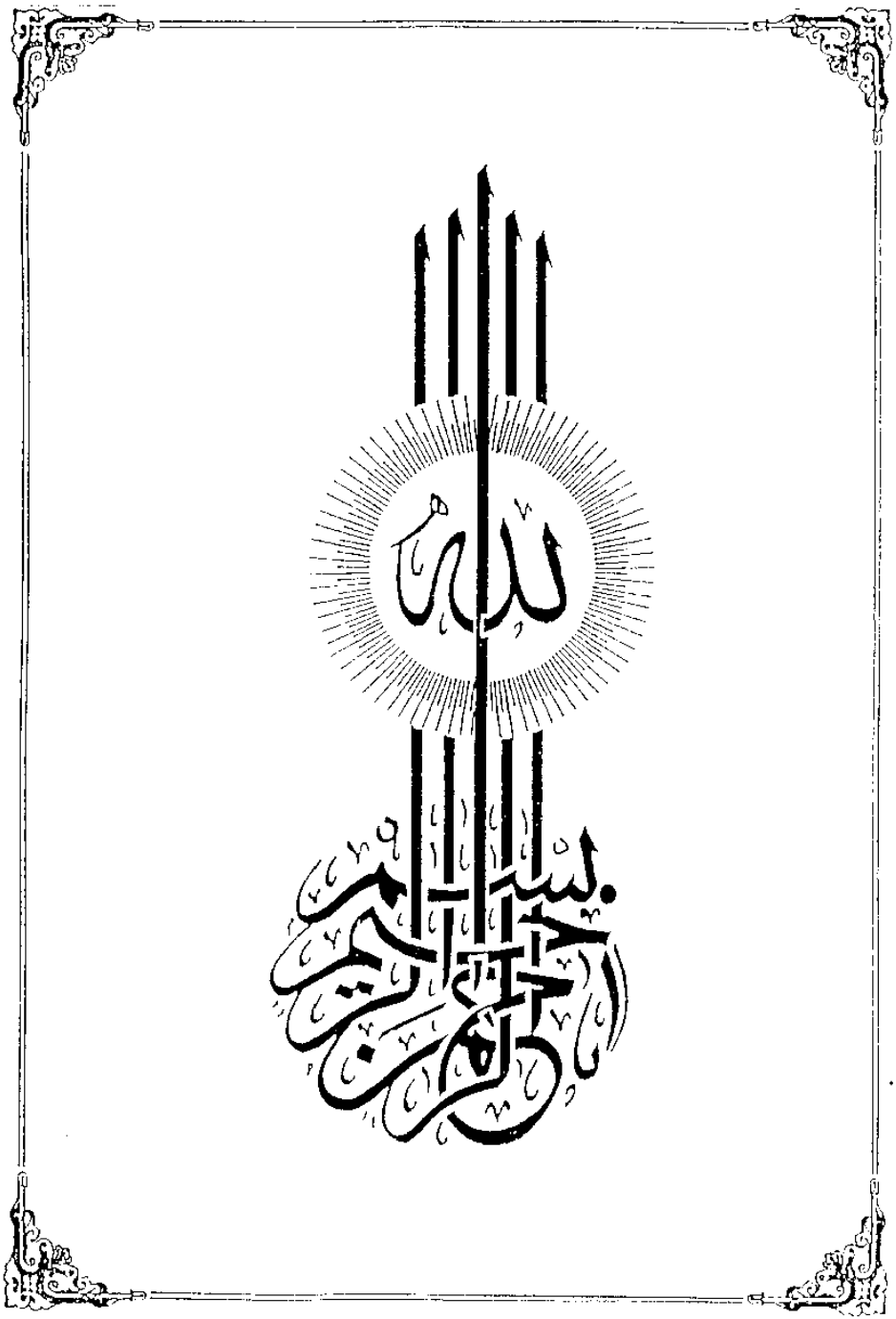
Dr. Nahela Ahmed Ibrahim
Lecturer in Clinical Pathology
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
1996

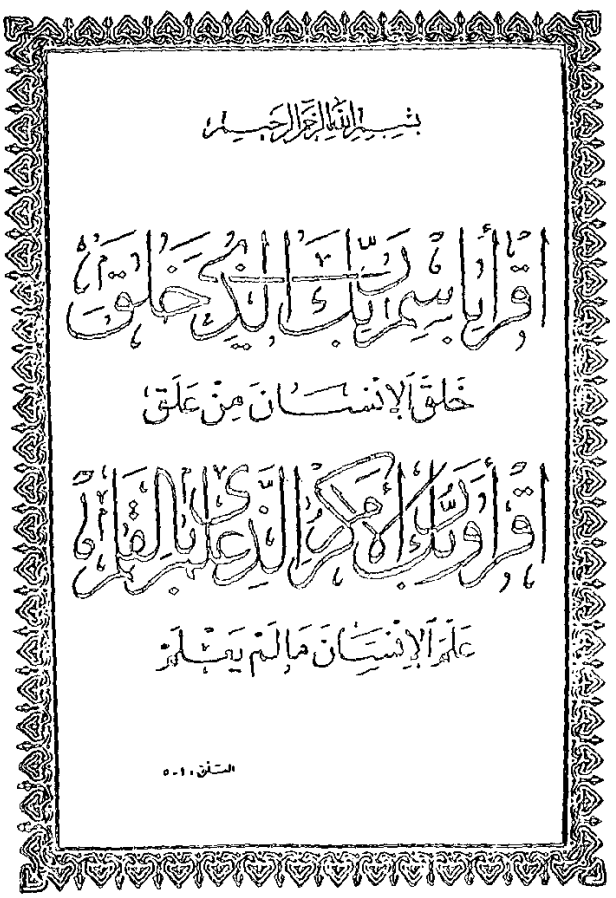
Central Library - Ain Shams University

منك ٤٠٢٨٨١٥

آمال
عبد الحميد



Central Library - Ain Shams University



Central Library - Ain Shams University

Central Library - Ain Shams University

ACKNOWLEDGEMENT

Words can never express may deepest gratitude and appreciation to **Prof. Dr. Fadila Hassan Sabry,** *Professor of Clinical Pathology, Ain Shams University, for her great supervision, unforgetable valuable generous advice and faithful guidance.*

My particular and deepest thanks to **Dr. Ihrahim Youssef,** *Lecturer in clinical pathology, Ain Shams University, who showed extraordinary care and guidance to me all through this study.*

I am grateful to **Dr, Nahella A. Shalabi,** *Lecturer in Clinical Pathology, Ain Shams University for her great support, great help and unending guidance in preparing and finishing this work.*

Last, but not least, no words could ever thank may family, may husband and may daughter who gave me a lot and received nothing.

Central Library - Ain Shams University

Central Library - Ain Shams University

LIST OF ABBREVIATIONS

APC	=	Activated protein c
APTT	=	Activated partial thromboplastin time
AT III	=	Antithrombin III
C_4b BP	=	C_4b binding protein
CPA	=	Capillary permeability to albumin
DIC	=	Disseminated intravascular coagulopathy
DM	=	Diabetes mellitus
EGF	=	Epidermal growth factor
FDPs	=	Fibrin degradation products
GLA	=	Gamma carboxy glutamic acid residue
HRG	=	Histidine rich glycoprotein
IDDM	=	Insulin dependent diabetes mellitus
INF	=	Interferone
LDL	=	Low density lipoprotein
NIDDM	=	Non insulin dependent diabetes mellitus
PC	=	Protein c
PCI	=	Protein c inhibitor
PGI_2	=	Prostaglandin I_2
PT	=	Prothrombin time
TFPI	=	Tissue factor pathway inhibitor
TM	=	Thrombomodulin
TNF	=	Tumor necrosis factor
TT	=	Thrombin time
UAE	=	Urinary albumin excretion
UPA	=	Urinary permeability to albumin
UUTMs	=	Urinary thrombomodulins
vWF	=	von Willebrand factor

Central Library - Ain Shams University

Central Library - Ain Shams University

LIST OF TABLES

Table (1): Distribution of thrombomodulin in several human tissues .....(28)

Table (2): Other markers of diabetic microangiopathy .....(66)

Table (3):
The studied paramters in the control group ...(89)

Table (4):
Correlation between TM and other parameters in control group .....(90)

Table (5):
Labordtory data of IDDM group .....(91)

Table (6):
Labordtory data of NIDDM group .....(92)

Table (7):
Relation of proteinuria to positivity of TM ..(93)

Table (8):
Comparison of TM value between patients with normal albuminuria and patients with microalbuminuria .....(93)

Central Library - Ain Shams University

Table (9):
Comparison of parameters studied between patients with microalbuminuria and patients with clinical nephropathy .....(94)

Table (10):
Relation of fundus changes to thrombomodulin positivity .....(95)

Table (11):
Correlation between TM and other parameters in IDDM group .....(95)

Table (12):
Correlation between TM and other parameters in NIDDM group .....(96)

Table (13):
Correlation between TM and other parameters in complicated patients of both IDDM and NIDDM group .....(96)

Table (14):
Correlation between TM and other parameters in noncomplicated patient of both IDDM and NIDDM groups .....(97)

Table (15):
Comparison between all parameters studied in all patients and control group .....(98)

Table (16a):
Comparison of all parameters between IDDM and control group .....(99)

Central Library - Ain Shams University

Table (16b):
Comparison of all parameters studied between complicated IDDM group and control group ....(100)

Table (17a):
Comparison of all parmeters studied between NIDDM group and the control group .....(101)

Table (17b):
Comparison of parameter studied between complicated NIDDM group and the control group .....(102)

Table (18):
Comparison between IDDM and NIDDM regarding all parameters studied .....(103)

Table (19):
Comparison of the studied parameters between noncomplicated patients with complicated patients .....(104)

Central Library - Ain Shams University

Central Library - Ain Shams University

CONTENTS

INTRODUCTION AND AIM OF THE WORK .....(1)

REVIEW OF LITERATURE

1- Natural anticoagulants:
- Normal Haemostasis .....(3)
- Natural anticoagulants .....(9)
  * Heparin/Antithrombin III .....(11)
  * Tissue factor pathyway inhibitor .....(11)
  * Protein C and protein s .....(13)

2- Thrombomodulin:
- Historical background .....(21)
- Structure .....(21)
- Distribution and forms .....(26)
- Function and interaction with coagulation factors .....(31)
- Regulation of TM expression .....(36)
- Thrombomodulin and disease .....(39)

3- Diabetic microangiopathy:
- Definition and classification of diabetes ..(42)
- Haematological changes in diabetes .....(43)
- Classification of complication of diabetes .(50)
- Microangiopathy in diabetes .....(52)

Central Library - Ain Shams University

- Theories of pathogenesis .....(52)
- Retinopathy .....(54)
- Nephropathy .....(57)
- Neuropathy .....(63)
- New markers of diabetic microangiopathy .....(64)

SUBJECT AND METHODS .....(67)

RESULTS .....(82)

DISCUSSION .....(122)

SUMMARY AND CONCLUSION .....(129)

RECOMMENDATIONS .....(132)

REFERENCES .....(133)

ARABIC SUMMARY.

Central Library - Ain Shams University