VON WILLEBRAND FACTOR (FVIIIR:AG) IN PEDIATRIC RHEUMATIC DISEASES

THESIS

Submitted in partial fulfilment of the

M.D. Degree in Pediatrics

By

SAHAR MOHAMED AHMED HASSANEIN

M.B. B.Ch. 1986, M.Sc. Ped. 1990

Supervisors

PROF. DR. AHMED SAMY KHALIFA

Professor of Pediatrics

Faculty of Medicine, Ain Shams University

PROF. DR. TARIF HAMZA SALLAM

Professor of Clinical Pathology

Faculty of Medicine, Ain Shams University

DR. AZZA ABDEL GAWAD ZAGHLOUL

Lecturer of Pediatrics

Faculty of Medicine, Ain Shams University

Faculty of Medicine

Ain Shams University

1993

ACKNOWLEDGEMENT

Thanks to ***GOD*** firstly and lastly.

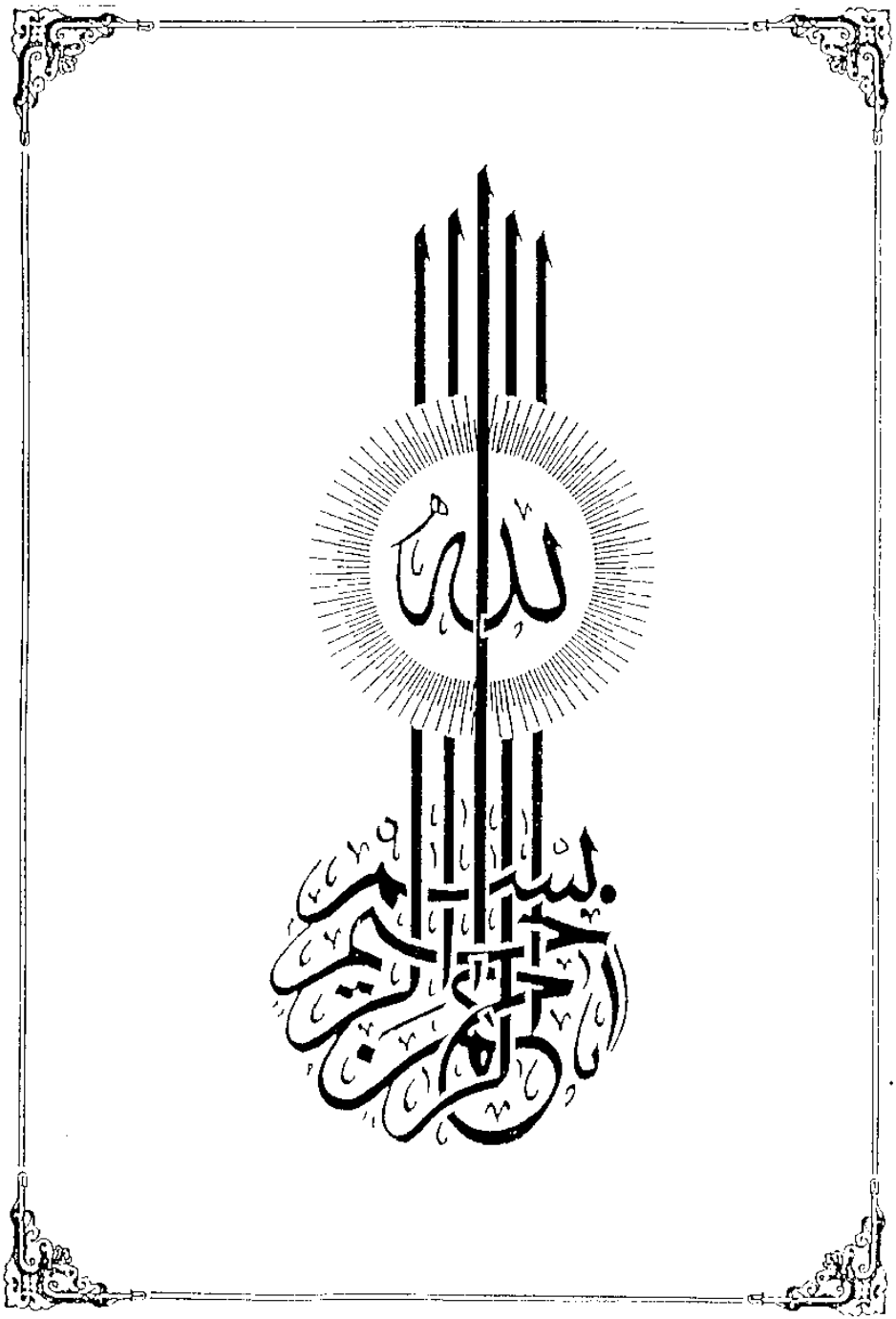
I wish to express my profound gratitude and sincere appreciation to **Prof. Dr. Ahmed Samy Khalifa**, for his valuable help, great care and encouragement.

I owe a debt of gratitude to **Prof. Dr. Tarif H. Sallam**, for his continuous help and continuous follow up.

I also wish to express my profound gratitude and sincere appreciation to **Dr. Azza Abdel Gawad**, for her unfailing advice and constructive supervision, which were of great importance in bringing this work to light.

I would also like to thank all **the patients and volunteers** in Ain Shams University, Children's Hospital.

Lastly, I would like to express my gratitude to **my family**.



CONTENTS

ABBREVIATIONS

ACL	Anticardiolipin antibody
ANA	Antinuclear antibody
Anti-Sm antibody	Anti-smooth muscle antibody
APL	Antiphospholipid
cDNA	Complementary deoxyribonucleic acid
CRP	C-reactive protein
DIC	Disseminated intravascular coagulopathy
ds DNS	Double stranded deoxyribonucleic acid
ESR	Erythrocyte sedimentation rate
FVIII:c	Factor VIII procoagulant activity
FVIIIR:Ag	Factor VIII related antigen
GP	Glycoprotein
Hb	Hemoglobin
HSP	Henoch Schönelin purpura
IL	Interleukin
JRA	Juvenile rheumatoid arthritis
Kb	Kilobase
KDa	Kilodalton
LA	Lupus anticoagulant
LE cells	Lupus erytheromatosus cells
MCTD	Mixed connective tissue disease
Mr	Molecular mass
mRNA	Messenger ribo-nucleic acid

OD	Optical density
PAN	Polyarteritis nodosa
PV	Plasma viscosity
RA	Rheumatoid arthritis
RER	Rough endoplasmic reticulum
RNP	Ribonucleoprotein
SDS	Sodium dodecyl sulfate
SLE	Systemic lupus erythematosus
TNC	Tumor necrosis factor
VDRL	Venereal disease research laboratory
VLDL	Very low density lipoprotein
vWD	von Willebrand disease
vWF	von Willebrand factor

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION AND AIM OF THE WORK

von Willebrand Factor (F VIII:R Ag) in Pediatric Rheumatic Diseases

Introduction

von Willebrand factor, also known as Factor VIII related Ag, is a multimeric glycoprotein which is an essential component in the clotting process. It is manufactured in the endothelial cells and megakaryocytes, and measurable amounts can be found in endothelial cells, platelets, and circulating in the plasma (*Girma et al.*, 1987).

Recently, abnormally high plasma levels of factor VIII:R Ag have been identified in patients with many rheumatic diseases of childhood including systemic juvenile arthritis, SLE, juvenile dermatomyositis and systemic vasculitis. The elevated levels of this protein are most likely a reflection of the existence of ongoing vascular damage due to active vasculitis (*Nusinow et al.*, 1984).

According to *Bowyer at al.* (1989), the elevated plasma levels of this factor in pediatric rheumatic disease has no correlation with the levels of ESR, C reactive protein or fibrinogen, suggesting that it is a more sensitive indicator of active systemic vasculitis than the other acute phase reactants.

It has been suggested that measurements of F VIII:R Ag in childhood rheumatic patients may be of great value in assessing the severity of systemic vascular involvement, in monitoring disease activity as well as an important prognostic factor (*James et al.*, 1990).

Aim of the Work

The aim of the present study is to determine the plasma level of von Willebrand factor in rheumatic diseases in pediatrics and to evaluate its significance as a marker of disease activity and as a prognostic factor.

REVIEW OF LITERATURE

RHEUMATIC DISEASES

The rheumatic diseases, inflammatory diseases of connective tissues or collagen diseases are disorders grouped together because of similarities in symptomatology and pathology. In general, they are associated with inflammatory changes in various connective tissues throughout the body, and extensive fibrinoid necrosis involving collagen. Many of the major rheumatologic disorders are autoimmune in nature. Deposition of immune complexes is an important feature of several of these diseases, and the immunoglobulin is believed to be an autoantibody (*Fye and Sack,* 1991).

Unknown factors in the environment act upon the immune system of patients who have inherited a predisposition to these diseases. Expression of disease is rarely seen in a familial pattern, although patients share common immunogenetic traits (*Hollister,* 1991).

The spectrum of rheumatic diseases in childhood are broad. Both arthralgia and true inflammatory synovitis may accompany any of the rheumatic diseases. A more significant common thread is the vascular disease, usually of inflammatory nature, found in all. Another common thread is the participation of immunologic mechanisms in their pathogenesis. Systemic lupus erythematosus (SLE), dermatomyositis, scleroderma and the vasculitides are not rare in children and constitute a significant segment of childhood disease (*Hanson,* 1985).