RELATION OF IgG RHEUMATOID FACTOR ISOTYPE TO RENAL AFFECTION IN SYSTEMIC LUPUS ERYTHEMATOSUS

Thesis

SUBMITTED FOR PARTIAL FULFILLMENT OF MASTER DEGREE IN PHYSICAL MEDICINE AND REHABILITATION

by

IMAN ABD EL HAMID KADDAH

M. B, B. CH

AIN SHAMS UNIVERSITY

Under Supervision of

Prof. Dr. NADIA ABD EL SALAM EL KADERY

ROFESSOR AND HEADMASTER OF PHYSICAL MEDICINE AND REHABILITATION DEPARTMENT

FACULTY OF MEDICINE

AIN SHAMS UNIVERSITY

Dr. NAGLAA ALI GAD ALLAH

Ass. Prof. OF PHYSICAL MEDICINE & REHABILITATION

FACULTY OF MEDICINE

AIN SHAMS UNIVERSITY

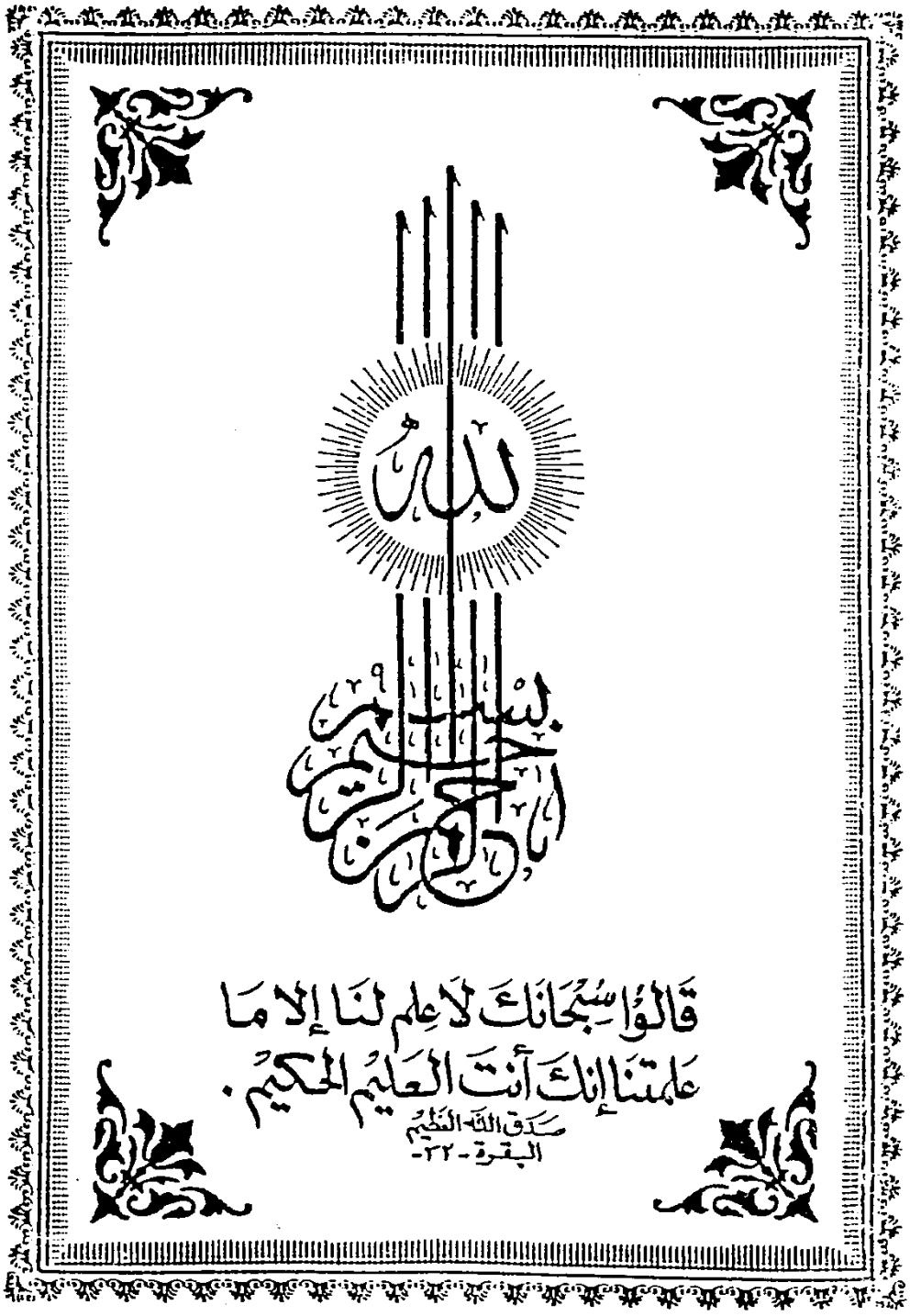
Dr. MONA MANSOUR HASAB EL NABY

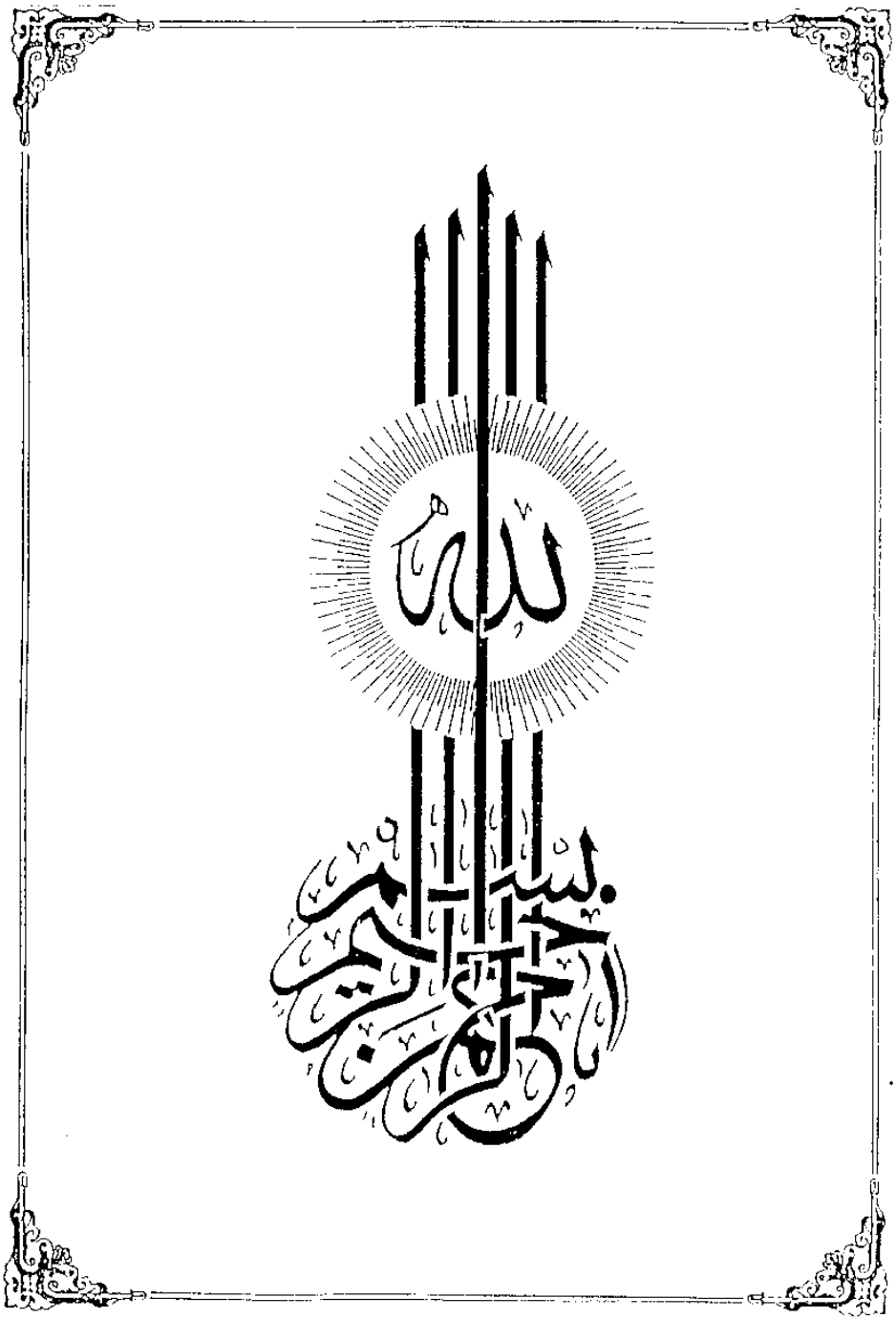
LECTURER IN PHYSICAL MEDICINE & REHABILITATION

FACULTY OF MEDICINE

AIN SHAMS UNIVERSITY

1995





Achnowledgement

I would like to express my deepest gratitude to **Prof. Dr. Nadia Abd El Salam El Kadery**, Professor and Head master of Physical Medicine and Rehabilitation department, Faculty of Medicine, Ain Shams University, for her mother's guidance, precious help and continous encouragment.

I'm also very grateful to **Dr. Naglaa Ali**, Ass. Prof. of Physical Medicine and Rehabilitation, Faculty of Medicine, Ain Shams University, for her expert supervision and generous support.

I would also like to express my sincere thanks to **Dr. Mona Mansour Hasab El Naby**, Lecturer of Physical Medicine and Rehabilitation, Faculty of Medicine, Ain Shams University, for her kind supervision continous discussion and fruitful criticism all throygh this work.

My deepest gratitude and appreciation, also, go to **Dr. Manal Hashem**, Lecturer of Clinical pathology, Faculty of Medicine, Ain Shams University who devoted her time and effort to conduct the practical phases of this work.

Last but not least, I would like to thank all the staff of Physical Medicine Department, Faculty of Medicine, Ain Shams University especially **Dr. Usama Heggy**, for their co - operation and encouragment.

To Everyone Taught Me a Letter

To my Parents

To My Husband

To My Son

LIST of ABBREVIATIONS

aCL	anti - cardiolipin .
AMLR	Autologous mixed lymphocyte reaction .
ANAs	Anti-nuclear antibodies
Anti - ds DNA	Anti - double stranded DNA .
Anti - ss DNA	Anti - single stranded DNA .
Anti - U1 RNP	Anti - uridine - 1 ribonucleo protein
Anti-Sm antibody	Anti - Smith antibody .
aPl - antibodies	anti - phospholipid antibodies .
APS	Anti - phospholipid antibody syndrome .
BUN	Blood urea nitrogen .
C1....C9	Complement- 1.....Complement - 9
CD4+	helper T - cells .
CH50	hemolytic complement .
CICS	circulating immune complexes .
CNS	central nervous system .
DBP	diastolic blood pressure .
DIL	drug - induced lupus .
DPGN	Diffuse Proliferative Glomerulonephritis .
DPLN	Diffuse Proliferarive Lupus Nephritis .
DVT	Deep Venous Thrombosis .
ECR-1	Erythrocyte complement receptor type - 1 .
ELISA	Enzyme - linked Immunosorbent Assay .
EPA	Eicoso Pentenoic Acid .
FPGN	Focal Proliferative Glomerulonephritis .
HMG Proteins	high mobility group proteins .
IC	Immune complex

IgA RF	Immunoglobulin - A isotype of Rheumatoid Factor .
IgD RF	Immunoglobulin - D isotype of rheumatoid factor .
IgE RF	Immunoglobulin - E isotype of rheumatoid factor .
IgG	Immunoglobulin - G
IgG RF	Immunoglobulin - G isotype of Rheumatoid Factor .
IgM	Immunoglobulin - M .
IgM RF	Immunoglobulin - M isotype of rheumatoid factor .
IL - 1	InterLeukin - 1 .
IL - 2	InterLeukin - 2 .
IL - 4	InterLeukin - 4 .
IL - 6	InterLeukin - 6 .
LAC	Lupus anticoagulant .
MCTD	Mixed connective tissue disease .
MPS	Mononuclear Phagocytic System .
NK Cells	Natural Killer Cells .
NPLE	Neuropsychiateric Lupus erthematosus .
PAPS	Primary antiphospholipid syndrome .
2^{o}APS :	Secondary antiphospholipid syndrome .
PMNS	Polymorphonuclear leucocytes .
RF	Rheumatoid Factor .
RIA	Radioimmunoassay .
RID	Radial Immunodiffusion .
RNP	Ribonucleoprotein
ScRNPs	Small cytoplasmic ribonucleoproteins .
SLE	System Lupus Erythematosus .
SnRNPs	Small nuclear ribonucleoproteins .

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INTRODUCTION

INTRODUCTION

SLE is a complex autoimmune multisystem disease characterized by occurance of a variety of autibodies **[Borg et al ., 1990]** .

Rheumatoid factors are autoantibodies directed against antigenic determinants on the Fc fragment of immunoglobulin G (IgG) molecules **[Carson , 1993]** .

The relation of RF to the presence of serious manifestations of SLE has gained much interest .

A protective role for RF against the development of lupus nephritis was first suggested by Davis and Bollet (1966) .

It was suggested that by competing with complement for binding with immune complexes , and thus minimizing their injurious properties , IgG RF plays this role **[Tarkowski & Westberg , 1987]** .

Demonstration of the reactivity of RF with soluble antigen - antibody complexes to form more heavily sedimenting immune precipitates has led to speculation that its role may involve formation of less soluble complexes easily phagocytosed and thus less likely to deposit in the renal glomeruli **[Turner - Stokes et al ., 1989]** .

It has been suggested again recently by **Howard et al . , (1991)** that there is a significant negative association between detectable rheumatoid factor at any time in a patient's course and clinically significant renal disease .

However , the concept of a protective role of RF against lupus nephritis is not universely accepted .

Houssiau et al . , (1991) did not find any differences in the frequency of RF is SLE patients with or without renal disease .

On the other extreme . **Miyazaki et al . , (1990)** reported that IgG , IgM and IgA RFs were significanthy increased in sera from patients with

diffuse proliferative lupus nephritis (DPLN) and that RFs could be detected bound to IgG on the renal glomeruli .

Moreover , it was reported that RF may play a role in the pathogen - esis of other manifestations of SLE . As a greater incidence of RF positivity was seen in SLE patients with Raynaud's phenomenon [**Gripenberg et al . , 1988**] , deforming arthropathy [**Segovia et al . , 1988**] and progressive cystic bone lesions **[Laasonen et al . , 1990]** .

AIM OF THE WORK

THE AIM OF THIS WORK

Is to conduct a clinical and laboratory study in patients with SLE in order to find the relation of IgG RF isotype to the various clinical manifestations especially renal disease.

REVIEW

Review

Systemic lupus erythematosus (SLE) is a chronic inflammatory disease appears to result from an immune regulatory disturbance brought about by the interplay of genetic , viral , environmental and hormonal factors **[Segovia, 1988]** .

Etiology of SLE :

I Genetic susceptibility :

SLE occurs in relatives of patients with the disease with a frequency between 0.4 % and 5 % , representing a several hundred fold increase over the incidence in the general population **[lehman et al ., 1979]**

Also , antinuclear antibodies (ANAs) have been found more frequently in relatives of SLE patients (3% - 44%) than in the general population (0 - 14 %) **[Cleland et al ., 1978] .**

Block and his colleagues (1976) have found that more than 50 % of seventeen monozygotic twin pairs appeared to be concordant for the disease . On the other hand the frequency of SLE in dizygotic twins is considerably lower . **[Arnett and Sculman , 1976]** .

Patients with discoid lupus were reported to have an increased frequency of HLA - B7 , whereas HLA- B8 predominated in patients with systemic disease and / or severe renal disease . **[Mikkelsen et al ., 1981]**

Furthermore , genes controlling the production of several complements are located within HLA region .

Deficiency of early complements , particularly C2 and C4 , is frequently associated with SLE and discoid lupus . **[Green et al ., 1986]** . In a study conducted by **Kemp et al (1987)** , 50 % of all caucasian SLE patients have been found to have a deletion of C4 A from one or both