C3d AS A MARKER OF NEONATAL SEPSIS

THESIS

Submitted for partial fulfilment of the

Master Degree in Pediatrics

By

MANAL RAGAB MOHAMED MOHAMED KHALIFA

M.B., B.Ch.

Under Supervision of

PROF. DR. GALILA MOHAMED MOKHTAR

Professor of Pediatrics

Faculty of Medicine – Ain Shams University

Assistant Supervisors

DR. ZEINAB AWAD EL-SAYED

Lecturer of Pediatrics

Faculty of Medicine – Ain Shams University

DR. RANDA ABD EL-WAHAB REDA

Lecturer of Clinical Pathology

Faculty of Medicine – Ain Shams University

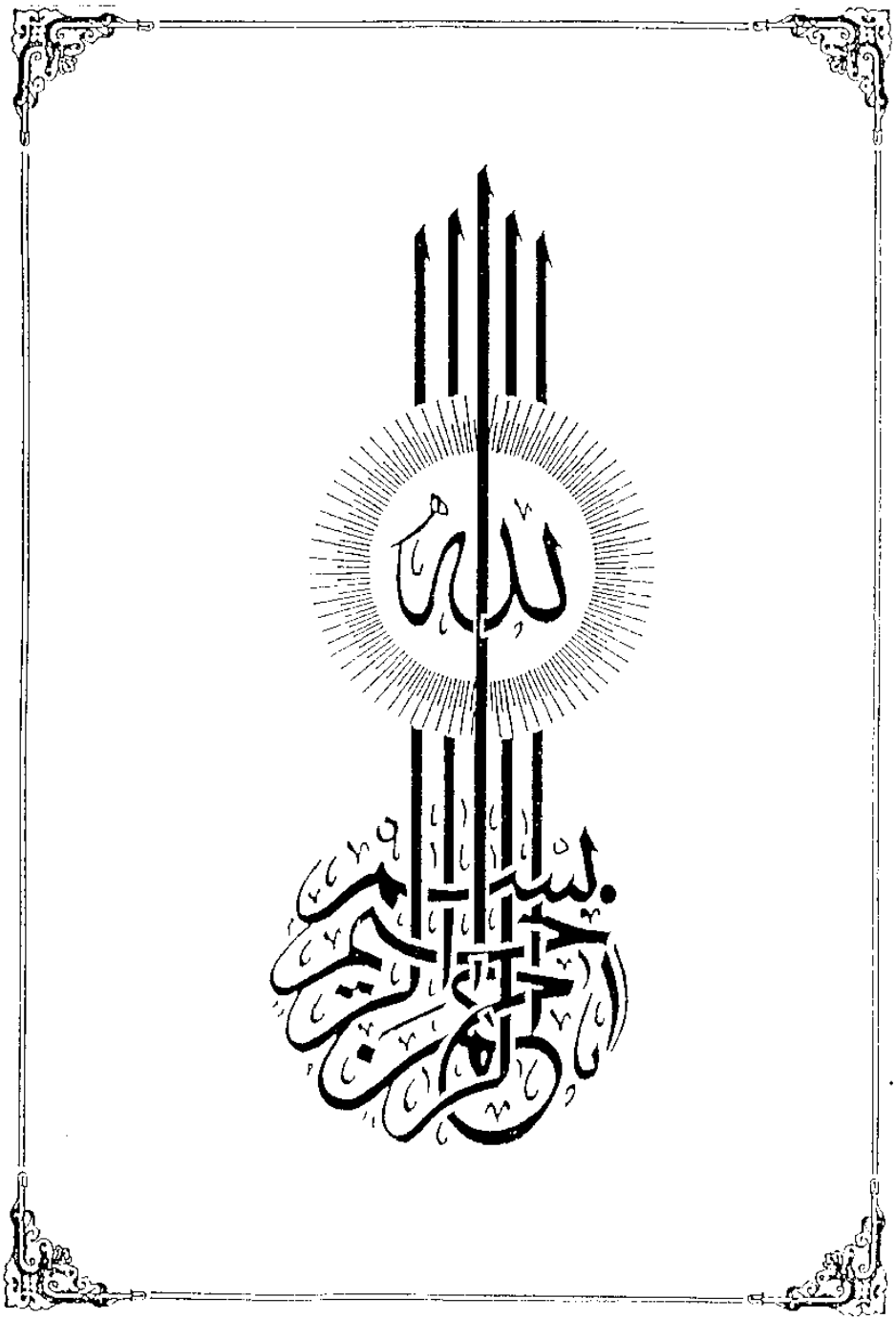
Faculty of Medicine

Ain Shams University

1995

To My Family ...

Whose love and encouragement made the beginning possible, and whose support and affection make everything also possible.



ACKNOWLEDGEMENT

Thanks to Allah.

I find no words by which I can express my extreme thankfulness, appreciation and profound gratitude to my great ***PROF. DR. GALILA MOKHTAR****, Professor of Pediatrics, Faculty of Medicine, Ain Shams University, for her generous help, guidance and kind encouragement.*

I would like to express my extreme indebtedness and thanks to ***DR. ZEINAB AWAD EL-SAYED****, Lecturer of Pediatrics, Faculty of Medicine, Ain Shams University, for her great help. Her generous guidance and continuous encouragement are highly appreciated.*

I am also greatly indebted to ***DR. RANDA REDA****, Lecturer of Clinical Pathology, Faculty of Medicine, Ain Shams University, for her great help and continuous support in the practical part of this work.*

Last, but not least, my deep thanks and best wishes are conveyed to the babies of this study as well as to their parents and to the staff members of the NICU of Gynecology and Obstetrics Hospital of Ain Shams University, to my colleagues and to everyone who participated in some way or another to let this work come to such a final picture, GOD bless them all.

Manal Ragab Khalifa

CONTENTS

LIST OF ABBREVIATIONS

α,1-ACT	Alpha, 1-antichemotrypsin
α,1-AGP	Alpha, 1-acid glycoprotein
α,1-AT	Alpha, 1-antitrypsin
α,1-GP	Alpha, 1-glycoprotein
Ab	Antibody
ADH	Antidiuretic hormone
Ag	Antigen
AGA	Appropriate for gestational age
ANC	Absolute neutrophilic count
BM	Bone marrow
C_3	The third component of complement
CFU	Colony-forming unit
CFU-G	Colony forming unit-granulocyte
CFU-GM	Colony forming unit-granulocyte monocyte
CFU-M	Colony forming unit-monocyte
CRP	C-reactive protein
CSF	Cerebrospinal fluid
CT	Computerized tomogrophay
DIC	Disseminated intravascular coagulation
DM	Diabetes mellitus
E coli	Escherichia coli
EACA	E-amino-n-caproic acid
ECG	Electrocardiogram
ECMO	Extracorporeal membrane oxygenation
EDRF	Endothelial derived relaxing factor
ESR	Erythrocyte sedimentation rate
F	Female
FRF	Fetal risk factor
G-CSF	Granulocyte-colony stimulating factor
GAB HS	Group A, beta hemolytic streptococcus
GBS	Group B-streptococcus
GE	Gastroenteritis
GIT	Gastrointestinal tract

GM-CSF	Granulocyte monocyte-colony stimulating factor
Hb	Hemoglobin
HFV	High frequency ventilation
HI	Hemophilus influenza
HPF	High power field
HPG	Haptoglobin
HSS	Hematological scoring system
I:T ratio	Immature to total neutrophil ratio
IFN-γ	Interferon gamma
Ig	Immunoglobulin
IL	Interleukin
IM	Intramuscular
IUGR	Intrauterine growth retardation
IV	Intravenous
IVIg	Intravenous immunoglobulin
KS	Kawasaki syndrome
LBW	Low birth weight
LCV	Leukocytoclastic cutaneous vasculitis
LN	Lymph nodes
LP	Lumbar puncture
M	Male
M-CSF	Monocyte-colony stimulating factor
MPO	Myeloperoxidase
MRF	Maternal risk factor
MW	Molecular weight
NEC	Necrotizing enterocolitis
NICU	Neonatal intensive care unit
NK	Natural killer
NS	Non-significant
NSP	Neutrophil storage pool
PAF	Platelet activating factor
PEG	Polyethylene glycol
PMNs	Polymorphonuclear neutrophils
PROM	Premature rupture of membrane
RA	Rheumatoid arthritis

RBC	Red blood cells
RDS	Respiratory distress syndrome
Rh	Rhesus factor
RID	Radial immunodiffusion
S. pneumoniae	Streptococcus pneumoniae
SD	Standard deviation
SGA	Small for gestational age
Sig	Significant
SS	Sepsis score
Staph. aureus	Staphylococcus aureus
TNF	Tumor necrosis factor
TXA_2	Thromboxan A_2
VAECMO	Venoarterial extracorporeal membrane oxygenation
WBCs	White blood cells
–ve	Negative
+ve	Positive

LIST OF TABLES

Page

LIST OF FIGURES

Introduction

INTRODUCTION

Systemic bacterial infections during the first month of life have remained a major cause of infant morbidity and mortality despite the development of broad spectrum antimicrobial agents and technologic advancements in life support therapy (*Yoder and Polin,* 1986).

Sepsis is a frequent complication of neonatal infections and the prognosis is still rather poor (*Bennet et al.,* 1981).

Acute phase reactants, notably fibrinogen, C-reactive protein (CRP) and orosomucoid (an alpha-1-acid glycoprotein) (α,1-AGP) have been used as markers for these infections. However, their use is not devoid of fallacies (*Hindocha et al.,* 1984).

Increased level of CRP without infection can be seen in cases with prolonged rupture of membranes, maternal fever during labour and perinatal asphyxia (*Kushner et al.,* 1973). *Ainbender et al.,* in 1982, added fetal distress, shock and meconium aspiration as other causes of rise in CRP. On the other hand, some authors pointed false negative results of CRP in cases of early infections as in Streptococcus B. This is a major drawback since Group B-Streptococcus (GBS) is frequently

incriminated in maternofetal infections and the mortality in these streptococcal infections was found to be greater when CRP was negative (*Sann et al.*, 1984).

Complement activation is an immune reaction that takes place during infection. Since C_3 is the central component in the complement system consequently the quantitation of C_3 split products in plasma of patients has been recently studied during infection. The level of the split product C_3d reflects the extent of complement activation, both by the classical and the alternative pathway. Furthermore, as C_3d diffuses rapidly into the plasma from sites of extravascular activation of complement, and has a slower turnover than C_3C, monitoring C_3d for evaluation of disease activity and complement activation dynamics has considerable advantages (*Brandslund et al.*, 1981).

Aim of the Work