CLINICAL UTILITY OF SERUM CHEMERIN IN PREGNANT WOMEN WITH PRE-ECLAMPSIA

Thesis

Submitted for Partial Fulfillment of Master Degree
in Clinical and Chemical Pathology

By

Noha Mohamed Ali Rasheed
M.B., B.Ch.
Ain Shams University

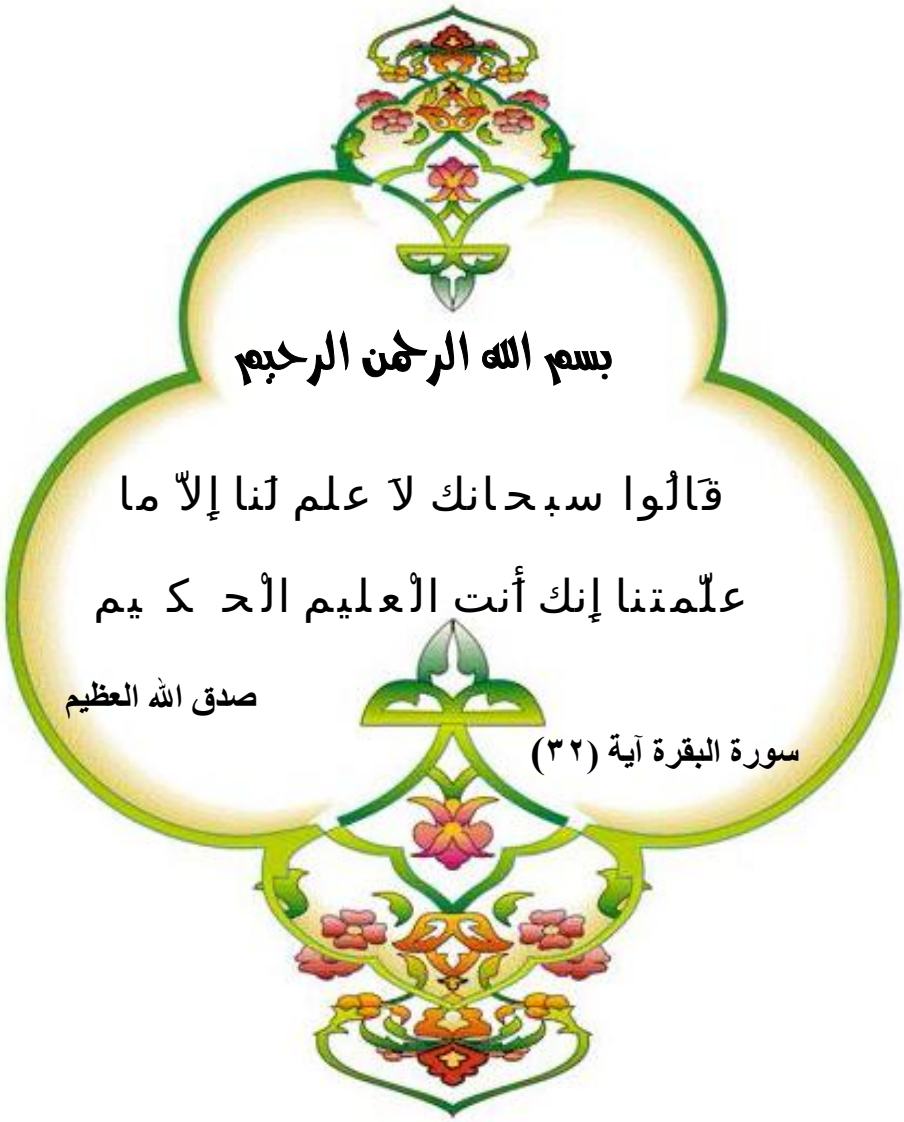
Under Supervision of

Prof. Dr./ Nadia Aly Abd El-Sattar
Professor of Clinical and Chemical Pathology
Faculty of Medicine – Ain Shams University

Prof. Dr./ Sayeda Abd El-Rahiem Saleh
Professor of Clinical and Chemical Pathology
Faculty of Medicine – Ain Shams University

Dr./ Noha Refaat Mohamed
Lecturer of Clinical and Chemical Pathology
Faculty of Medicine – Ain Shams University

Faculty of Medicine
Ain Shams University
2013


بسم الله الرحمن الرحيم
قَالُوا سبحانك لاَ علم لَنا إلاّ ما
علّمتنا إنك أنت الْعليم الْحكيم
صدق الله العظيم
سورة البقرة آية (٣٢)

Acknowledgment

First and foremost, I feel always indebted to Allah, the Most Merciful, Who gives me power to accomplish this work.

I would like to express my deepest appreciation and sincere gratitude to ***Prof. Dr./ Nadia Aly Abd El-Sattar,*** *Professor of Clinical and Chemical Pathology, Faculty of Medicine – Ain Shams University for her sincere help, constant encouragement, constructive criticism, and valuable guidance, I was truly honoured to work under her supervision.*

I feel deeply indebted to ***Prof. Dr./ Sayeda Abd El-Rahiem Saleh,*** *Professor of Clinical and Chemical Pathology, Faculty of Medicine – Ain Shams University for her active cooperation, deep concern, enthusiastic encouragement, and the effort and time she has devoted to the fulfillment of this work.*

I would like to acknowledge ***Dr./ Noha Refaat Mohamed,*** *Lecturer of Clinical and Chemical Pathology, Faculty of Medicine – Ain Shams University, for supervising the work, continuous advice and support.*

I owe special thanks to My Family, for their care, patience and continuous encouragement.

Noha Mohamed Ali Rasheed

Contents

List of Abbreviations

AAP : Aminoantipyrine
ACE : Angiotensin-converting enzyme
ACOG : American College of Obstetrics and Gynecology
ALT : Alanine aminotransferase
AM : Adrenomedullin
ANG II : Angiotensin-converting enzyme II
AST : Aspartate trasaminase
AT1 : Angiotensin II receptor-1
ATP : Adenosine triphosphate
C 15 : Chemerin 15
CBC : Complete blood picture
CCRL2 : Chemokine (C-C motif) receptor-like 2
CD4 : Cluster of differentiation 4
CD8 : Cluster of differentiation 8
cDNA : Complementary deoxyribonucleic acid
CE : Cholesterol esterase
CHOD : Cholesterol oxidase
CMKLR1 : Chemokine-like receptor 1
CRP : C-reactive protein
CSF : Cerebrospinal fluids
CTBs : Cytotrophoblasts
CV : Coefficient of variation
DBP : Diastolic blood pressure
DCs : Dendritic cells
DGAT2 : Diacylglycerol acetyltransferase
DIC : Disseminated intravascular coagulation
DM : Diabetes mellitus
DNA : Deoxyribonucleic acid
EC : Endothelial cells
EDTA : Ethylene diaminetetraacetic acid
ELISA : Enzyme linked immunosorbent assay
eNOS : Endothelial nitric oxide synthase
ET-1 : Endothelin-1
FFA : Free fatty acid
FITC : Fluorescein isothiocyanate
FP : False positive
FSH : Follicle-stimulating hormone
GA : Gestational age

List of Abbreviations *(Cont...)*

GGT : Gamma-glutamyl transferase
GK : Glycerol kinase
GLUT4 : Glucose transporter 4
GnRH : Gonadotropin-releasing hormone
GPO : Glycerol Phosphate oxidase
GPR1 : G-protein coupled receptor 1
HDL-C : High-density lipoprotein-cholesterol
HELLP : Hemolysis, elevated liver enzymes and low plateles
HEVs : High endothelial venules
IFN-γ : Interferon-gamma
IGF : Insulin-like growth factor
IL-15 : Interleukin-15
IL-1β : Interleukin- 1 beta
IL-2 : Interleukin-2
IL-6 : Interleukin-6
IL-8 : Interleukin-8
IRS-1 : Insulin receptor substrate-1
KDa : Kilo Dalton
LDH : Lactate dehydrogenase
LDL-C : Low-density lipoprotein-cholesterol
LE : Lupus erythematous
LH : Luteinizing hormone
LPL : Lipoprotein lipase
LPS : Lipopolysaccharide
MAHA : Microangiopathic hemolytic anemia
MMP 2/9 : Matrix metalloproteinase- 2/9
MMP-13 : Matrix metalloproteinase-13
MMPs : Matrix metalloproteinases
mRNA : Messenger ribonucleic acid
NAD : Nicotinamide adenine dinucleotide
NADP : Nicotinamide adenine dinucleotide phosphate
NCP : Nitrocellulose paper
NK : Natural killer cells
NO : Nitric oxide
NOS : Nitric oxide synthase
PAI-1 : Plasminogen activator inhibitor-1
PAPP-A : Pregnancy associated plasma protein-A
PCR : Polymerase chain reaction

List of Abbreviations *(Cont...)*

PDGF : Platelet derived growth factor
PlGF : Placental growth factor
POD : Peroxidase
PP-13 : Placental protein-13
PPAR γ : Peroxisome proliferator-activated receptor gamma
RARRE2 : Retinoic acid receptor responder protein 2
RAS : Rennin angiotensin system
RT-PCR : Reverse transcriptase PCR
SBP : Systolic blood pressure
SD : Standard deviation
SDS-PAGE : Separated by polyacrylamide gel electrophoresis.
SDS-PAGE : Sodium dodecyl sulfate- polyacrylamide gel electrophoresis
sEng : Soluble endoglin
sFlt1 : Soluble Fms-like tyrosine kinase-1
TG : Triglycerides
TIG2 : Tazarotene-induced gene 2 protein
TN : True negative
TNF-α : Tumor necrosis factor -alpha
tPA : Tissue plasminogen activator
TTP : Thrombotic thrombocytopenic purpura
uPA : Urokinase plasminogen activator
VEGF : Vascular endothelial growth factor
VEGFR-1 : Vascular endothelial growth factor receptor-1
VLDL : Very low density lipoprotein

List of Tables

List of Tables *(Cont...)*

List of Figures

List of Figures *(Cont...)*

INTRODUCTION

Pre-eclampsia, is a multisystem disorder specific to pregnant women. It is characterised primarily by new-onset hypertension and proteinuria. It remains one of the most important causes of maternal and fetal mortality and morbidity worldwide ***(Stepan et al., 2011).***

The complete pathogenesis of this disease still remains unclear, underlining a multifactorial etiology.Deficient remodeling of the spiral arteries during the interaction between maternal and fetal sides at the time of trophoblast invasion has been postulated as a cause of placental insufficiency. This would lead to the release of inflammatory factors in the systemic maternal circulation ***(Young et al., 2010).*** In addition, ***Arikan et al., (2010)*** reported that adipokines may play an important role in the pathogenesis of pre-eclampsia through their role in low-grade systemic inflammation, atherosclerosis, and insulin resistance. Therefore, it is reasonable to suppose that adipokines may directly or indirectly influence the function of placental endothelial cells.

Chemerin, is a novel adipokine, also known as tazarotene-induced gene 2 protein (TIG2) and retinoic acid receptor responder protein 2 (RARRES2) ***(Duan et al., 2011).*** It is a 14 KDa secretory adipokine, expressed mainly in adipose tissues, macrophages, liver and lungs ***(Bozaoglu et al., 2010).***

Many studies demonstrated that chemerin is a potent angiogenic factor and induce gelatinolytic activity of endothelial cell ***(Kaur et al., 2010).*** Moreover, it has recently been reported that circulating chemerin levels have a close association with insulin resistance, lipid metabolism and hypertension ***(Ress et al., 2010).***

AIM OF THE WORK

The aim of the present study is to assess serum chemerin in a group of pregnant females with pre-eclampsia to evaluate its clinical utility in diagnosis and assessment of severity of the disease. This will facilitate the development of a predictor test that may help in developing novel strategies for the treatment of pre-eclampsia.