

# **Serum Placental Growth Factor in Early Second Trimester for Prediction of Pre-Eclampsia**

**Thesis**

*Submitted for Partial fulfillment of  
Master degree in Obstetrics and Gynecology*

**By**

**Manal Salem Abdullah Alyasser**

*M.B.,B.Ch., (2006)  
El-Mergeb University  
Faculty of Medicine – AL-Khoms – Libya  
Resident in Al-khoms Hospital*

**Under Supervision of**

**Prof. Hassan Awwad Bayoumy**

*Professor of Obstetrics and Gynecology  
Faculty of Medicine- Ain Shams University*

**Prof. Nahla Mohamed Zakaria Yousef**

*Professor of Clinical and chemical Pathology  
Faculty of Medicine- Ain Shams University*

**Dr. Ihab Adel Gomaa**

*Lecturer of Obstetrics and Gynecology  
Faculty of Medicine- Ain Shams University*

**Faculty of Medicine  
Ain Shams University  
2012**

# عامل النمو المشيمي بمصل الدم فى بداية الثلوث الثانى للحمل للتنبؤ بتسمم الحمل

رسالة

مقدمة من

الطبيبة/ منال سالم عبد الله اليسير

تحت إشراف

أ.د. / حسن عواد بيومى

أستاذ أمراض النساء والتوليد

كلية الطب - جامعة عين شمس

أ.د. / نهلة محمد زكريا يوسف

أستاذ الباثولوجيا الإكلينيكية والكيمائية

كلية الطب - جامعة عين شمس

د/ إيهاب عادل جمعة

مدرس أمراض النساء والتوليد

كلية الطب - جامعة عين شمس

كلية الطب

جامعة عين شمس

٢٠١٢



*First and foremost, I'd like to thank **Allah**, the creator of the heavens and the earth and what's between them, to Him, whose knowledge is beyond all knowledge, for blessing this work until it has reached its end, as a part of His generous help throughout my life...*





*I am greatly honored to express my utmost thanks to **Prof. Hassan Awwad Bayoumy**, Professor of Obstetrics and Gynecology, Faculty of Medicine Ain Shams University, for his constructive supervision, generous guidance & giving me such an honor to work under his supervision.*

*I would like to express my sincere gratitude & appreciations to **Prof. Nahla Mohamed Zakaria Yousef**, Professor of Clinical and chemical Pathology, Faculty of Medicine, Ain Shams University, who gave me enormous support, advice and encouraged me to go on, dedicated much of her precious time to me.*

*My deepest feelings, gratitude, appreciation and every thankful feeling go to **Dr. Ihab Adel Gomaa**, Lecturer of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University for his close supervision, continuous help and the tremendous effect he had done in the meticulous revision of the whole work*

*Last but not least, I would like to thank all the members of our department for their encouragement and support, all the patients and nursing staff.*

 **Manal**



**To**

**My Beloved Husband and my Family**

*Who gave me too much  
And received too little*





## List of Contents

<i>Title</i>	<i>Page No.</i>
<b>List of Tables</b> .....	iii
<b>List of Figures</b> .....	v
<b>List of Abbreviations</b> .....	vii
<b>Protocol</b> .....	- -
<b>Introduction</b> .....	1
<b>Aim of the work</b> .....	5
<b>Review of literature</b> .....	6
Pre-eclampsia.....	6
Risk factors of pre-eclampsia .....	7
Pathophysiology.....	12
Classification of pre-eclampsia .....	16
Severity of pre-eclampsia .....	17
Eclampsia.....	18
Etiology of pre-eclampsia .....	18
Placental origin of pre-eclampsia .....	23
Pathogenesis of pre-eclampsia: .....	29
Diagnosis of pre-eclampsia.....	33
Complications of pre-eclampsia.....	37
Prediction of pre-eclampsia .....	42
Prevention of pre-eclampsia.....	53
Management of pre-eclampsia .....	55

---

## List of Contents *(Cont...)*

<i>Title</i>	<i>Page No.</i>
Placental growth factor (PLGF) .....	65
Patients and methods.....	70
Results.....	80
Discussion .....	101
Summary and Conclusion .....	109
Recommendations.....	112
References .....	113
Arabic summary.....	



## List of Tables

<i>Table No.</i>	<i>Title</i>	<i>Page No.</i>
1	Classification of hypertensive disorders complicating pregnancy .....	8
2	Risk factors for pre-eclampsia .....	11
3	Indications of severity of pre-eclampsia .....	17
4	Diagnostic criteria for pre-eclampsia .....	36
5	Maternal and fetal complication in severe pre-eclampsia .....	41
6	Below is listed a typical example of a standard curve with the DRG PLFG ELISA .....	77
7	Distribution of pregnant women according to blood pressure .....	80
8	Clinical characteristics of study group .....	81
9	Laboratory findings of study group .....	81
10	PLGF level at 15-20 weeks of study group .....	85
11	Level of PLGF in mild and severe pre-eclampsia .....	86

## List of Tables *(Cont..)*

<i>Table No.</i>	<i>Title</i>	<i>Page No.</i>
12	Level of PLGF according to the onset of pre-eclampsia.....	87
13	Comparison between early and late onset pre-eclampsia .....	88
14	Correlation between PLGF and different variables in normotensive and pre-eclampsia groups.....	89
15	Define the area under the ROC curve to detect pre-eclampsia.....	91
16	Sensitivity, specificity, predictive values of positive and negative for prediction of pre-eclampsia .....	91

## List of Figures

<i>Figure No.</i>	<i>Title</i>	<i>Page No.</i>
1	Placentation abnormalities in pre-eclampsia.....	15
2	A framework for systematic reviews of the underlying mechanism of pre-eclampsia .....	22
3	The diagram presents an overview of early trophoblast development.....	23
4	The diagram represents the early development of the trophoblast lineage.....	26
5	Pathogenic consideration in the development hypertensive disorders due to pregnancy .....	32
6	Flt1 on endothelial cells with few sFlt1 in the circulation .....	68
7	Mean BMI in the two groups .....	82
8	Mean blood pressure in the two groups .....	82
9	Mean birth weight in the two groups.....	82
10	Mean AST and ALT in the two groups .....	84
11	Mean serum creatinine in the two groups .....	84

## List of Figures *(Cont...)*

<i>Figure No.</i>	<i>Title</i>	<i>Page No.</i>
12	Box plot representing PLFG in the two groups.....	85
13	Box plot representing PLFG in mild & severe pre-eclampsia.....	86
14	Box plot representing PLFG in early and late pre-eclampsia.....	87
15	Scatter diagram showing direct correlation between PLGF and 24-h urinary protein.....	90
16	Scatter diagram showing direct correlation between PLGF and mean arterial pressure.....	90
17	Receiver operating characteristic (ROC) curve to define the best cut-off value of placental growth factor for prediction of pre-eclampsia. ....	92

## **List of Abbreviations**

ACOG .....	American College of Obstetricians and Gynecologist
AFP .....	Alpha feto protein
ALT .....	Alanine aminotranferase
ANP .....	Aterial naturetic peptide
AST .....	Aspartate aminotransferase
AUC .....	Area under the curve
BMI .....	Body mass index
BP .....	Blood pressure
BPP .....	Biophysical profile
BUN .....	Blood urea nitrogen
cGMP .....	cyclic Guanosine Monophosphate
CT .....	Computerized Tomography
DBP .....	Diastolic blood pressure
DES .....	Diethyl stilbesterol
DIC .....	Disseminated intravascular coagulation
ELISA .....	Enzyme linked immunosorbent assay
FGR .....	Fetal growth restriction
GA .....	Gestational age
HELLP .....	Hemolysis, elevated Liver function tests, and low platelets
hsCRP .....	High sensitive c- reactive protein
IUGR .....	Intrauterine growth restriction
KIRs .....	Killer immunoglobulin receptors
LDH .....	Lactate dehydrogenase
MAP .....	Mean arterial pressure
mmHg .....	Millimeter mercury
MRI .....	Magnetic Resonant Image
mRNA .....	Messenger ribonucleic acid

## **List of Abbreviations** *(Cont...)*

NHBPEPWG...	National High Blood Pressure Education Program Working Group
NICE .....	National institute for health and clinical excellence
NPV .....	Negative predictive value
NST .....	Non stress test
P.C.....	Post conception
P.M.....	Post menstruation
PAI-I.....	Plasminogen activator inhibitor-I
PAPP-A.....	Pregnancy associated plasma protein A
PE .....	Pre-eclampsia
PIH .....	Pregnancy induced hypertension
PLGF .....	Placental growth factor
Plt .....	Platelet count
PP 13.....	Placental protein 13
PPV .....	Positive predictive value
PTX 3.....	Pentraxin 3
ROC .....	Receiver Operating Characteristic
SBP.....	Systolic blood pressure
sEng.....	Soluble Endoglin
sFlt1.....	Soluble Fms-Like tyrosine kinase -1
SGA.....	Small for gestational age
SGOT .....	Serum glutamate oxaloacetic transaminase
SGPT .....	Serum glutamate pyruvate transaminase
SHBG .....	Sex hormone binding globulin
SLE.....	Systemic Lupus Erythematosus
SPSS.....	Statistical package for social sciences
TAT .....	Thrombin anti thrombin III

## **List of Abbreviations** *(Cont...)*

Th .....	Helper-T-cells
Th1 .....	Helper T cells type 1
Th2 .....	Helper T cells type 2
TNF- $\alpha$ .....	Tumor necrotic factor –alpha
TTP.....	Thrombotic Thrombocytopenic Purpura
TxA2 .....	Tromboxane A2
U/S .....	Ultrasound
UK.....	United Kingdom
VEGF .....	Vascular endothelial growth factor
VEGFR-I....	Vascular endothelial growth factor receptors-I
VEGFR-II ..	Vascular endothelial growth factor receptors-II
VPF .....	Vascular permeability factor
WHO .....	World health organization
Wks .....	Weeks