Serum Triglyceride Level and Uterine Artery Pulsatility Index in Pre-eclampsia and Normal Pregnancy

Chesis

Submitted for partial fulfillment of Master degree of Obstetrics and Gynecology

By

Marwa El Sayed Mahmoud El Sayed

(M.B., B.Ch, Alexanderia University, 2003) (Resident of Obstetrics and Gynecology at AbouKir General Hospital)

Under supervision of

Prof. / Mohamed Hassan Nasr El Dein

Professor of Obstetrics and Gynecology Faculty of Medicine, Ain Shams University

Dr. /Amr Mohamed El Helaly

Assistant Professor of Obstetrics and Gynecology Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
2014



I am immensely grateful to **Prof Dr. Mohemed Hassan Nasr El Deín**, Professor of Obstetrics and
Gynecology, Faculty of Medicine, Ain Shams
University for his sincere guidance and continuous
encouragement during the course of this work.

I would like to express my deep gratitude to **Dr. Amr Mohamed El Helaly**, Assistant Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University. Without his continuous guidance, support, encouragement and assistance, the accomplishment of this work wouldn't have been possible.

I'm grateful to **Dr. Engy Samy Abdel Gawad**, and all the staff of ultrasound and fetal care unit, Demerdash Hospital, Ain Shams University, who helped me throughout this work. I'm grateful to the patients for whom all our efforts are devoted.

Also I would like to express my deep feelings and thanks to my husband and my kids whose patience and support helped me to complete this work.



Contents

Subjects Page	
List of abbreviations	
• List of Tables	III
• List of Figures	V
List of Picture	VIII
• Introduction	1
Aim of the work	5
• Review of Literature	
Chapter (1): Pre-Eclampsia	6
Chapter (2): Triglycerides	89
Chapter (3): Doppler Ultrasound	99
Patients & methods	122
• Results	130
• Discussion	143
• Summary	151
Conclusion & Recommendations	154
• References	155
Arabic summary	

List of Abbreviations

ACL : Anticardiolipin antibodies

AFLP : Acute fatty liver of pregnancy

AFP : Alpha fetoprotein

AST : Asparate transaminase

BUN : Blood urea nitrogen

CDE : Color doppler energy

CDI : Color doppler imaging

eNOS : Endothelial nitric oxide synthase

EVT : Extravillous trophoblast

FAT : Fatty acid transporter

GFR : Glomerular filtration rate

GWS: Genome wide scanning

HCG : Human chorionic gonadotrophin

HDLP: High density lipoprotein

: Hemolysis, elevated liver enzymes, low *HELLP*

platelets

HIFs : Hypoxia-inducible transcription factors

HLA : Human leukocyte antigen

IgG : Immunoglobulin g

IgM : Immunoglobulin m

KIR : Killer immunoglobulin receptor

LAC : Lupus anticoagulant

LDA : Low dose aspirin

🕏 List of Abbreviations 🗷

LDL : Low density lipoprotein

NDMA : N-methyl d-aspartate

NK : Natural killer

PAPP-A: Pregnancy-associated plasma protein a

PI: Pulsatility index

PIGF : Placental growth factor

PIH : Pregnancy induce hypertension

PP13 : Placenta protein 13

: Posterior reversible leukoencephalopathy

PRES syndrome

PTH : Parathyroid hormone

RI : Resistance index

S/D : Systole/diastole

sEng : Soluble endoglin

sFlt-1 : Soluble fms-like tyrosine kinase 1

SLE : Systemic lupus erysematosis

SPNs : Single-nucleotide polymorphisms

 $\beta 2$ -GP-I : $\beta 2$ glyco protein i

TG : Triglycerides

TGF : Transforming growth factor

: Thrombotic thrombocytopenic purpura-

hemolytic uremic syndrome

UPPVI: Utero-placental vascular insufficiency

VEGF : Vascular endothelial growth factor

VLDL : Very low density lipoprotein

🕏 List of Tables 🗷

List of Tables

Tables	Title	Page
No.	Title	No.
Table (1)	Criteria for diagnosis of preeclampsia.	10
Table (2)	The presence of one or more of the	11
	following criteria are features of severe	
	preeclamptic disease.	
Table (3)	Criteria for diagnosis of gestational	12
	hypertension.	
Table (4)	Factors associated with an increased	15
	risk of developing preeclampsia.	
Table of Results		
Table (1)	Comparison between the two studied	130
	groups regarding gestational age.	
Table (2)	Comparison between the two studied	131
	groups regarding age.	
Table (3)	Comparison between the two studied	132
	groups regarding systolic BLP.	
Table (4)	Comparison between the two studied	133
	groups regarding diastolic BLP.	
Table (5)	Comparison between the two studied	134
	groups regarding BMI.	

🕏 List of Tables 🗷

Tables	Title	Page
No.	Title	No.
Table (6)	Comparison between the two studied	135
	groups regarding T.G.	
Table (7)	Comparison between the two studied	136
	groups regarding PI.	
Table (8)	Comparison between the two studied	137
	groups regarding proteinuria	
Table (9)	Correlation between different studied	138
	items in group I(cases).	
Table (10)	Correlation between different studied	139
	items in group II(controls).	

🕏 List of Figures Z

List of Figures

Figure No.	Title	Page No.
Figure (1)	Showing the four major hypertensive	7
	disorders related to pregnancy.	
Figure (2)	Showing the clinical picture of pre-	18
	eclampsia.	
Figure (3)	Showing abruption placenta.	32
Figure (4)	Digram for pathogenesis of	34
	preeclampsia.	
Figure (5)	Diagram of anchoring villi (AV) at the	35
	maternal-fetal interface in normal	
	pregnancy.	
Figure (6)	Abnormal placentation in preeclampsia.	37
Figure (7)	Single Nucleotide Polymorphisms in G	45
	Protein Signaling Pathway Genes in	
	Preeclampsia.	
Figure (8)	For calcium metabolism in	46
	preeclampsia.	
Figure (9)	Showing endothelial dysfunction in	51
	preeclampsia.	
Figure (10)	For pathogenesis of pre-eclampsia.	52

🕏 List of Figures 🗷

Figure No.	Title	Page No.
Figure (11)	Showing early prediction to	56
	preeclampsia.	
Figure (12)	For expectant management of pre-	79
	eclampsia.	
Figure (13)	Showing the chemical structure of	89
	triglyceride.	
Figure (14)	Showing the metabolism of triglycerides	92
Figure (15)	Continuous wave Doppler.	101
Figure (16)	Pulsed wave Doppler.	103
Figure (17)	Sites of insonation of uterine artey.	113
	Adapted from.	
Figure (18)	Non-pregnant uterine artery Doppler	114
	waveform.	
Figure (19)	Doppler phases of the uterine artery	116
	during normal pregnancy.	
Figure (12)	Normal uterine artery PI with gestation.	120
Figure (13)	Normal (left) and abnormal (right) flow	121
	velocity waveforms from the uterine	
	arteries at 24 weeks of gestation. (S=	
	peak systolic; D= End diastolic).	

🕏 List of Figures 🗷

Figure No.	Title	Page No.
Figures of Results		
Figure (1)	Comparison between the two studied	130
	groups regarding gestational age.	
Figure (2)	Comparison between the two studied	131
	groups regarding age.	
Figure (3)	Comparison between the two studied	132
	groups regarding systolic BLP.	
Figure (4)	Comparison between the two studied	133
	groups regarding diastolic BLP.	
Figure (5)	Comparison between the two studied	134
	groups regarding BMI.	
Figure (6)	Comparison between the two studied	135
	groups regarding T.G.	
Figure (7)	Comparison between the two studied	136
	groups regarding PI.	
Figure (8)	Comparison between the two studied	137
	groups regarding proteinuria.	

🕏 List of Picture 🗷

List of Picture

Figure No.	Title	Page No.
Picture (1)	Light and Electron microscopy of	25
	glomerular endotheliosis	
Picture (2-A)	Hemolytic anemia	27
Picture (2-B)	Helmet cells in microangiopathic	27
	hemolytic anemia.	

Introduction

Pre-eclampsia occurs in about 3-5% of pregnancies and is an important cause of fetal and maternal morbidity and mortality worldwide (*Magnuseen et al.*, 2007).

Pre-eclampsia occurs during second and third trimester of pregnancy and it is more common in nulliparous women. It is characterized by blood pressure of 140/90 mmHg or rise in systolic blood pressure of more than 30 mmHg or diastolic blood pressure of more than 15 mmHg after 20 weeks of gestation, in conjugation with proteinuria >300 mg/24 hours or greater or equal to 1+ or 100 mg/dl by dipstick response (*Gary et al.*, 2005).

Hypertriglyceridemia, traditionally defined as a serum or plasma triglyceride (TG) concentration above1.6mmol/l, is found in13% of woman aged 20-40 years (*Maclean et al.*, 1999).

The association of alteration of serum lipid profile in preeclampsia is well documented. Known to be strongly associated with atherosclerotic cardiovascular diseases and has a direct effect on endothelial dysfunction. The most important feature in preeclampsia is hypertension which is supposed to be due to vasospastic phenomenon in kidney, uterus, placenta and brain (*Singh et al.*, 2006).

Altered lipid synthesis leading to decrease in PGI2:TXA2 ratio is also supposed to be an important way of pathogenesis in pregnancy induced hypertension (*Dutta & Kunar*, 2001).

Thus, abnormal lipid metabolism seems important in the pathogenesis of preeclampsia. Pre-eclampsia and related disorders are known to affect function of various organs involved in lipid and lipoprotein metabolism. Several studies have shown that endothelial dysfunction is related to hyperlipidemia (*Dutta & Kunar*, 2001).

Significantly elevated plasma concentration of triglycerides (TG) were found in women with pre-eclampsia in comparison to normal pregnancy (*Sattar et al.*, 2000).

Plasma lipids and lipoproteins increase during pregnancy. The mechanism for pregnancy-induced changes in lipids is not completely understood, but appears to be partly caused by elevated estrogen, progesterone and human placental lactogen (Wiznitzer et al., 2009) & (Mankuta et al., 2010).

Lipid levels in women with pre-eclampsia are reported to be higher than those in healthy pregnant women (*Sahu et al.*, 2009 & *Khoury et al.*, 2009).

Women with pre-eclampsia present arterial lesions at the uteroplacental implantation site. These morphological lesions are usually observed in cases of acute atherosclerosis, and are characterized by areas with fibrinoid necrosis surrounded by lipid-laden macrophage (*Ross*, 1999).

These microscopic lesions are similar to atherosclerosis found outside pregnancy. Lipid deposits are also seen in the glomeruli of pre-eclamptic patients, a finding known as glomerular endotheliosis. Glomerular lesions are associated with proteinuria, a predictive indicator and marker of disease severity (*Airoldi & Weinstein*, 2007). It has also been suggested that triglycerides may be involved in this renal damage (*Winkler et al.*, 2003).

The severity of both hypertension and proteinuria seems to reflect the degree of endothelial damage (*Sahu et al.*, 2009). The possible correlation between the altered lipid profile and the severity of renal lesions, as reflected by proteinuria, may contribute towards clarify the complex pathophysiology of preeclampsia.

Pregnancy is associated with physiologic hyperlipidemia, and in normal pregnancy, this feature is not atherogenic that is believed to be under hormonal control (*Winkler et al., 2003*). Women who develop preeclampsia, experience more dramatic lipid changes compared with normotensive women.

Also patients with hyperlipidemia, especially hypertriglyceridemia have a higher incidence of and are prone to develop more severe cases of preeclampsia (*Enquobahrie et al.*, 2004).

The pulsatility index (PI) of the uterine artery is an indirect measure of vascular resistance in the uteroplacental circulation (*Roberts & Gammill*, 2006).

There is a positive relationship between vascular dysfunction and adverse pregnancy outcomes such as preeclampsia. Hence, changes in the uterine artery PI have been used to predict pre-eclampsia (*Roberts & Gammill, 2006*).

Uterine artery Doppler evaluation provides important information on the normal physiological transformation of subplacental arteries. The transformation of the spiral and radial arteries is normally complete at 20 to 24 weeks of gestation (*Catov et al.*, 2007).

Uteroplacental vascular impedance decreases gradually during vessel transformation, but is fairly stable after 24 weeks of gestation (*Magee et al.*, 2008).

Increased uteroplacental vascular impedance after 24 weeks of gestation is strongly related to the development of pre-eclampsia later in pregnancy (*Melchiorre et al.*, 2008).