

FIRST-TRIMESTER 3-DIMENSIONAL POWER DOPPLER OF THE UTEROPLACENTAL CIRCULATION AND PLACENTAL VOLUME IN PREDICTING ADVERSE PREGNANCY OUTCOMES

Thesis

Submitted for partial fulfillment of MD
in Obstetrics and Gynecology

By

Mohamed Mahmoud Abd El-Hamid

M.B.B.Ch December 2009

M. Sc. 2014 in Obstetrics and Gynecology – Ain Shams University

Assistant Lecturer of Obstetrics and Gynecology

Ain Shams University Maternity Hospital

Supervised by

Dr. Gasser Adly El-Bishry

Professor of Obstetrics and Gynecology

Faculty of Medicine – Ain Shams University

Dr. Amgad El-Said Abou Gamrah

Professor of Obstetrics and Gynecology

Faculty of Medicine – Ain Shams University

Dr. Mohamed Samir Sweed

Assistant Professor in Obstetrics and Gynecology

Faculty of Medicine – Ain Shams University

Dr. Gihan El-Sayed El-Hawwary

Lecturer in Obstetrics and Gynecology

Faculty in Medicine – Ain Shams University

**Faculty of Medicine
Ain Shams University
2017**

Acknowledgement

First of all and foremost, deep thanks to “ALLAH”; and the most merciful for his grace and mercy for giving me the effort to complete this work.

Words are few to speak and do fail to express my deepest gratitude to ***Dr. Gasser Adly El-Bishry***, Professor of Obstetrics and Gynecology, Faculty of medicine, Ain Shams University, for his continuous attention, follow up and providence of all facilities possible to complete this work, without his honest assistance and abundant patience, this work would have never come to light.

I would like to express my deep appreciation and most gratefulness for ***Dr. Amgad El-Said Abou Gamrah***, Assistant Professor of Obstetrics and Gynecology, Ain Shams University, for his constant guidance, experienced advice and great encouragement which have been of the most important.

A great appreciation and most gratefulness for ***Dr. Mohamed Samir Sweed***, Assistant Professor of Obstetrics and Gynecology, Ain Shams University, for his continuous guidance and, big patience, experienced advice and great encouragement which has been of the most valuable and to whom I will always be indebted.

I acknowledge with much gratitude to ***Dr. Gihan El-Sayed El-Hawwary***, Lecturer of Obstetrics and Gynecology, Faculty of Medicine – Ain Shams University, for her great supervision and unlimited help to provide all facilities to accomplish this work.

I would like also to express my great thanks to ***Ultrasound Special fetal Care Unit*** and especially ***Dr. Monira Ali Ali*** for her great effort during the whole work.

Last but not least, thanks to all my patients and their families for their cooperation and help during the whole work.

 ***Mohamed Mahmoud Abd El Hamid***

List of Contents

<i>Subject</i>	<i>Page No.</i>
List of Abbreviations	i
List of Tables.....	iii
List of Figures	v
Introduction	1
Aim of the Work.....	4
Review of Literature	
Chapter (1): Placental Development and Imaging	5
Chapter (2): Adverse Pregnancy Outcomes.....	34
Chapter (3): 3D Ultrasound Physics and Basis and 3D Power Doppler	69
Patients and Methods.....	85
Results.....	95
Discussion	115
Conclusion.....	126
Recommendations	127
Summary	128
References	132
Arabic Summary	—

List of Abbreviations

<i>Abbr.</i>	<i>Full-term</i>
ACTH	Adrenocorticotrophic Hormone
AUCs	Area Under the Curves
BPD	Bi Parietal Diameter
BPP	Biophysical Profile
BMI	Body Mass Index
CRH	Corticotropin Releasing Hormone
CRL	Crown Rump Length
CT	Computed Tomography
CW	Continuous Wave
2D	2Dimensional
3DPD	3Dimensional Power Doppler
EDD	Expected Date of Delivery
EDV	End Diastolic Volume
FGR	Fetal Growth Restriction
FI	Flow Index
FL	Femoral Length
FMH	FetoMaternal Hemorrhage
GH	Gestational Hypertension
GPA	Gravid Para Abortus
HCG	Human Chorionic Gonadotropin
HCS	Human Chorionic Somatotropin
HELLP	Hemolysis, Elevated Liver enzymes, Low Platelets
HIV	Human Immunodeficiency Virus
HPA	Hypothalamic Pituitary Adrenal
IUGR	Intrauterine Growth Restriction
Kg	Kilogram
IgG	Immunoglobulin G
IVF	InVitro Fertilization
LBW	Low Birth weight

LH	Luteinizing Hormone
LMP	Last Menstrual Period
MCA	Middle Cerebral Artery
mmHg	Millimeter of Mercury
MRI	Magnetic Resonance Imaging
NHBPEP	National High Blood Pressure Education Program
PE	Preeclampsia
PI	Pulsatile Index
PIH	Pregnancy-Induced Hypertension
PPROM	Premature Preterm Rupture of Membranes
PSV	Peak Systolic Velocity
PTL	Preterm Labor
PV	Placental Volume
PW	Pulsed Wave
RI	Resistance Index
ROC	Receiver Operator Characteristics
SD	Standard Deviation
SGA	Small for Gestational Age
SLE	Systemic Lupus Erythromatosis
SPSS	Statistical Program for Social Science
TAMV	Time-Average Maximum Velocity
US	Ultrasound
VFI	Vascularization Flow Index
VI	Vascularization Index
VOCAL	Virtual Organ Computer-aided Analysis
WHO	World Health Organization
Wks	Weeks
UA	Umbilical Artery
μmol	Micromole

List of Tables

<i>Table No.</i>	<i>Title</i>	<i>Page No.</i>
Table (1):	Descriptive statistics for the study population as regards their basic demographic data	98
Table (2):	Descriptive statistics for the indices of 3D power Doppler study of uteroplacental circulation and placental volume	100
Table (3):	Summary of incidence of adverse pregnancy outcomes in the study population	101
Table (4):	Comparison between patients who developed preeclampsia and those who didn't regarding 3D power Doppler indices	103
Table (5):	Receiver-operating characteristic (ROC) curve analysis for prediction of preeclampsia using VI, FI, VFI or placental volume.....	105
Table (6):	Comparison between patients who developed gestational hypertension and those who didn't regards 3D power Doppler indices.	107
Table (7):	Comparison between patients who developed fetal growth restriction and those who didn't regards 3D power Doppler indices.	108
Table (8):	Receiver-operating characteristic (ROC) curve analysis for prediction of fetal growth restriction using VI, FI, VFI or placental volume.	110
Table (9):	Comparison between patients who suffered preterm labor and those who didn't regards 3D power Doppler indices.....	112

Table (10):	Comparison between patients who suffered intrauterine fetal demise and those who didn't regards 3D power Doppler indices	113
Table (11):	Comparison between patients who developed placental abruption and those who didn't regards 3D power Doppler indices	114

List of Figures

<i>Figure No.</i>	<i>Title</i>	<i>Page No.</i>
Figure (1):	Placenta	6
Figure (2):	Steps of implantation	7
Figure (3):	Sectional plan of the gravid uterus in the third and fourth month.....	9
Figure (4):	Diagram showing earliest observed stage of human ovum.....	10
Figure (5):	Diagram illustrating early formation of allantois and differentiation of body-stalk.....	10
Figure (6):	Diagram showing later stage of allantoic development with commencing constriction of the yolk-sac	10
Figure (7):	Diagram showing the expansion of amnion and delimitation of the umbilicus	10
Figure (8):	Diagram illustrating a later stage in the development of the umbilical cord	11
Figure (9):	Diagrammatic a. Primary b. Secondary chorionic villi	13
Figure (10):	A full-term placenta.	16
Figure (11):	Placental circulation.....	18
Figure (12):	Normal placenta. US image shows a placenta (P) that is relatively homogeneous in echotexture. The retroplacental clear space is hypoechoic	23
Figure (13):	a) Transverse transabdominal US image shows the hyperechoic placenta (*) surrounded by the hypoechoic myometrium (arrowheads) (b) Sagittal transabdominal US image shows a	

thin, hypoechoic line (arrowheads) at the inner aspect of the myometrium representing a subplacental clear space (c) Sagittal transabdominal US image shows a normal organized pattern of subplacental blood flow that parallels the myometrium (<i>Baughman et al., 2008</i>).	24
Figure (14): Transverse images of the placenta (P)	25
Figure (15): Measurement of placental thickness	27
Figure (16): Grade 0	28
Figure (17): Grade 1	29
Figure (18): Grade 2	29
Figure (19): Grade 3	30
Figure (20): Placenta, power Doppler, 3D Ultrasound image ...	32
Figure (21): The umbilical cord inserts into an anterior placenta but an umbilical vessel extends into the amniotic membranes	32
Figure (22): 3D ultrasound image of the placenta	33
Figure (23): The four stage model of preeclampsia	40
Figure (24): Pathophysiological changes in preeclampsia.....	42
Figure (25): Doppler indices derived from the maximum frequency shift envelope	75
Figure (26): (A) Three-dimensional structure of the placenta at 12 weeks of gestation generated using the VOCAL technique (B) Histogram analysis of the placenta	84
Figure (27): Three-dimensional power Doppler (3DPD) volume analysis.....	84
Figure (28): General Electric TM Voluson E6 ultrasound machine	88

Figure (29): Three-dimensional structure of the placenta at 12 weeks of gestation generated using the VOCAL technique	89
Figure (30): Histogram analysis of the placenta	91
Figure (31): CONSORT 2010 flow diagram showing the recruitment and handling of the study population during the course of the study.....	96
Figure (32): Box Plots of age, BMI and GA of the study population.	99
Figure (33): Box Plot showing distribution of various 3D power Doppler indices..	100
Figure (34): Box Plot showing distribution of placental volume.....	100
Figure (35): Bar graph summarizing incidence of adverse pregnancy outcomes in study population.....	101
Figure (36): Grouped bar graph summarizing 3D power Doppler indices and placental volume in development of preeclampsia.	103
Figure (37): ROC curve analysis for prediction of preeclampsia using FI	106
Figure (38): ROC curve analysis for prediction of preeclampsia using VFI	106
Figure (39): ROC curve analysis for prediction of preeclampsia using VI.....	106
Figure (40): Grouped bar graph summarizing 3D power Doppler indices and placental volume in development of gestational hypertension.	107
Figure (41): Grouped bar graph summarizing 3D power Doppler indices and placental volume in development of fetal growth restriction.	108

Figure (42): ROC curve analysis for prediction of fetal growth restriction using FI.....	111
Figure (43): ROC curve analysis for prediction of fetal growth restriction using VI.....	111
Figure (44): ROC curve analysis for prediction of fetal growth restriction using VFI.....	111
Figure (45): Grouped bar graph summarizing 3D power Doppler indices and placental volume in development of preterm labor.....	112
Figure (46): Grouped bar graph summarizing 3D power Doppler indices and placental volume in occurrence of intrauterine fetal demise.	113
Figure (47): Grouped bar graph summarizing 3D power Doppler indices and placental volume in development of placental abruption.....	114



Introduction

The placenta is named for its appearance after the Greek” *plakuos*”, meaning “flat cake” and is responsible for the nutritive, respiratory, and excretory functions of the fetus. The placenta is often overlooked in the routine evaluation of a normal gestation, receiving attention only when an abnormality is detected (*Hill, 2008*).

Development of the placenta is a highly regulated process that is essential for normal fetal growth and development, and for maintenance of a healthy pregnancy. The placenta fulfills several critical roles as the interface between mother and fetus: it prevents rejection of the fetal allograft, enables respiratory gas exchange, transports nutrients, eliminates fetal waste products, and secretes peptide and steroid hormones (*Aplin, 2000*).

The human placenta is a highly invasive and proliferative structure during the first half of pregnancy. While the growth rate of the human placenta decreases, its maturation continues throughout gestation (*Arroyo and Winn, 2008*).

Abnormal placental development is associated with a few obstetrical adverse outcomes, such as fetal growth restriction, preterm labor, preeclampsia, fetal hypoxia and death (*Cnossen et al., 2008*).

Adverse pregnancy outcomes, including Preeclampsia (PE), preterm birth (PTB), low birth weight (LBW), intrauterine growth restriction (IUGR), and stillbirth, are important events determining neonatal morbidity and mortality. Newborn infants from pregnancies affected by one of these events can develop severe long-term disabilities as well as problems due to neonatal intensive care (**Kramer, 1987**).

Three-dimensional (3D) ultrasound can provide improved imaging of fetal anatomy compared with conventional 2D ultrasound. Specifically, novel assessment of the placenta by 3D ultrasound is more available than 2D ultrasound, including surface-rendering imaging and volume measurement. With the recent advances in 3D power Doppler ultrasound, as well as quantitative 3D Power Doppler histogram analysis, quantitative and qualitative assessments of the vascularization and blood flow of the placenta have become feasible (**Hata et al., 2004**).

Uteroplacental and fetoplacental perfusion have been extensively studied throughout gestation and after delivery, in order to understand the pathogenetic mechanisms underlying adverse pregnancy outcomes including preeclampsia, intrauterine growth restriction (IUGR) and other adverse pregnancy outcomes. Direct investigation of the perfusion of *in-vivo* placentae has become possible using three-dimensional (3D) power Doppler sonography (**Matijevic and Kurjak, 2002**).

Thanks to great technological progress over the last few years, it is now possible to quantitatively evaluate intraplacental blood circulation and placental volume by

means of 3D Power Doppler and Virtual Organ Computer-aided Analysis (VOCAL) technique (*Yu et al., 2003*).

Even very small blood movements within the investigated volume can be detected by a combination of power and color Doppler sonography, and their impact in the given volume, representing the overall perfusion, is evaluated by indices computed by built-in algorithms. In the placenta, these indices potentially reflect both uteroplacental and fetoplacental blood flow. These two vasculatures can be indirectly and separately evaluated by conventional Doppler velocimetry (*Papageorghiou et al., 2004*).

Intraplacental blood circulation is described by three vascular indices: vascularization index (VI), flow index (FI), and vascularization flow index (VFI). Vascularization index is the ratio of the number of color voxels (volumetric pixel) to the total number of voxels in the sampled tissue, thus it represents the percentage of vascularized tissue. Flow index is the average color value of all color voxels and it describes the mean velocity of flow in the sampled tissue. The vascularization-flow index is the average color value of all color and gray voxels and describes both: the vascularization and the blood flow (*Merce' et al., 2004*).

So far, only a small number of studies evaluating placental vasculature with the use of 3D Power Doppler technique have been conducted. They differed from one another in respect of the applied methodologies of measuring the placental vasculature and placental volume (*Merce' et al., 2005*).