First Trimester Uterine Artery Doppler, Placental Volume and Ductus Venosus Blood Flow as Predictors of Second Trimester Fetal Growth

Thesis
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قياس دوبلر الشريان الرحمي و حجم المشيمة و معدل سريان الدم في القناة الوريدية الجنينية في الثلث الأول من الحمل للتنبؤ بالنمو الجنيني في الثلث الثاني من الحمل

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LIST OF ABBREVIATIONS

Abbreviation	Meaning
2D	2-dimensional
3D	3-dimensional
AC	Abdominal circumference
AFP	Maternal serum alpha fetoprotein
AGA	Appropriate for gestational age
BPD	Biparietal diameter
cm	centimeter
COH	Controlled ovarian hyperstimulation
CRH	Corticotropin-releasing hormone
CRL	Crown-rump length
dB	Decibel
DV	Ductus venosus
FL	Femur length
FVW	Flow velocity waveforms
HC	Head circumference

LIST OF ABBREVIATIONS (continued)

HCG	Human chorionic gonadotropin
Hz	Hertz
ICSI	Intracytoplasmic sperm injection
IQ	Intelligence quotient
IUGR	Intrauterine growth restriction
IVF	In-vitro fertilization
LGA	Large for gestational age
mm	millimeter
MoM	Multiples of the median
MRI	Magnetic resonance imaging
NT	Nuchal translucency
OFD	Occipito-frontal diameter
P	Probability
PAPP-A	Pregnancy-associated plasma protein A
PET	Positive emission tomography
PI	Pulsatility index

LIST OF ABBREVIATIONS (continued)

PQ	Placental quotient
PRF	Pulse repetition frequency
PVIV	Peak velocity index for veins
RI	Resistance index
s	second
S/D ratio	Systolic/Diastolic ratio
SD	Standard deviation
SGA	Small for gestational age
SPECT	Single photon emission computed tomography
TDE	Tissue Doppler echocardiography
UAD	Uterine artery Doppler
VOCAL	Virtual Organ Computer-Aided AnaLysis

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INTRODUCTION AND AIM OF THE WORK

Introduction

Intrauterine growth restriction (IUGR) continues to be an important determinant of perinatal mortality and morbidity in modern obstetrics *(Kady & Gardosi, 2004)*. Physical evidence of abnormal fetal growth becomes typically apparent in the second half of pregnancy *(Gluckman et al., 1992)*, although recent studies have suggested that indicators of aberrant growth may be present as early as in the first trimester *(Smith, 2004)*.

During normal pregnancy, invading trophoblast ensures the vascular remodeling of the uterine spiral arteries necessary to cause the physiological increase in blood supply to the intervillous space needed for pregnancy. Defective trophoblastic invasion of the spiral arteries is associated with subsequent development of IUGR, preeclampsia and other associated complications. In these pregnancies, the uteroplacental circulation remains in a state of high resistance, which causes generalized endothelial cell injury, compromising vascular integrity and an atherosis-like process in the small arteries resulting in vessel occlusion, local ischemia and necrosis *(Pijnenborg et al., 2006)*. This can be measured noninvasively by Doppler ultrasound *(Campbell et al., 1983)*.

Uterine artery Doppler measurements show that impedance to flow in the uterine arteries decreases with gestational age in normal pregnancies; that impedance to flow is increased in established IUGR *(Ducey et al., 1987)*; and that this increased impedance predates the onset of the clinical syndrome of

IUGR *(Papageorghiou et al., 2004)*. There have been a number of studies that have examined the ability of uterine artery Doppler velocimetry to predict complications of impaired placentation. Most have used uterine artery Doppler in the second trimester. Examination of the uterine circulation in the first trimester in order to predict IUGR and preeclampsia, however, has increasingly been reported *(Papageorghiou & Campbell, 2006)*. In a study by *Prefumo et al. (2004)*, patients undergoing termination of pregnancy in the first trimester had uterine artery Doppler measurements of resistance to blood flow. In this study, the proportion of decidual vessels with endovascular trophoblastic invasion was significantly higher in those with low resistance compared with those with high resistance to blood flow.

In *1995*, *van den Elzen et al.* reported a study of 352 women aged 35 years and older. Using Doppler studies, the pulsatility index was measured at 12-13 weeks of gestation. When the pulsatility index was in the upper quartile, the risk for IUGR was doubled when compared with women in which the pulsatility index was in the lower quartile.

Wegrzyn et al. (2005) stated that in a normal pregnancy there is a doubling in placental volume between 11 and 14 weeks of gestation, which is accompanied by a simultaneous doubling in fetal size and gestational sac volume. The introduction of three-dimensional (3D) ultrasound has made it possible to measure placental volume. There is some evidence from in vitro studies that in the estimation of volumes of an irregular object, such as the placenta, the VOCAL (Virtual Organ Computer-aided AnaLysis) technique may be more accurate.

Three-dimensional studies have reported that reduced placental volume in the first and second trimesters is associated with the subsequent development of IUGR *(Metzenbauer et al., 2001)*. Placental size has also been described as being different in pregnancies with aneuploidies. *Stoll et al. (1998)* examined nearly 400 Down syndrome fetuses and reported that their placentas at term were considerably smaller than those of unaffected pregnancies.

The ductus venosus has long been discussed as being a main distributor of oxygenated blood in the fetus *(Rudolph, 1985)*. It is a narrow trumpet-shaped vein with an isthmic entrance, which remains narrow throughout the last half of pregnancy *(Kiserud et al., 1991)*. *Hecher and Hackeloer (1997)* suggested that changes in the DV blood flow pattern precede the appearance of abnormal fetal heart rate patterns in pregnancies complicated by placental insufficiency. Since IUGR is thought to be associated with placental compromise and hypoxia, Doppler evaluation of the ductus venosus blood flow for prediction of IUGR appears to be worth evaluating in the first trimester.

Aim of the work

The aim of this study is to assess the potentials of first trimester (11 to 13+6 weeks) evaluation of uterine artery Doppler, placental volume and ductus venosus blood flow in the prediction of second trimester (20 to 24 weeks) fetal growth parameters.

The ability to predict subsequent abnormal fetal growth in the first trimester could enable more appropriate fetal surveillance and management, which potentially might reduce perinatal complications due to fetal growth abnormalities.