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

Hesham Fekry Ahmed
Lecturer of Obstetrics and Gynecology
Department of Obstetrics and Gynecology, Faculty of Medicine, Al-Azhar University
E-MAIL: Manofegypt28@yahoo.com

Abstract

To evaluate the potentials of the first trimester uterine artery Doppler, placental volume measurement and ductus venosus blood flow as predictors of third trimester fetal growth parameters. This study was a prospective-observational study, conducted on 200 pregnant women, during a period of 2 years starting from June 1st 2013 till May 30th 2015, in order to evaluate the potentials of the first trimester uterine artery Doppler, placental volume measurement and ductus venosus blood flow as predictors of third trimester fetal growth parameters, as well as to determine whether these measurements are independent or not in the prediction of fetal growth restriction. First trimester uterine artery pulsatility index (PI) was found to have a negative correlation with third trimester BPD, HC, AC and FL, as well as with fetal birth weight. First trimester placental volume was found to have a positive correlation with third trimester HC, AC and FL but not with BPD. No correlation was found between first trimester placental volume and fetal birth weight. First trimester ductus venosus Doppler indices (PI and PVIV) were found to have no correlation with third trimester fetal growth parameters (BPD, HC, AC and FL), which was later confirmed at birth.

Keywords

Uterine artery Doppler; ductus venosus; pulsatility index; intrauterine insemination
I. Introduction

Intrauterine growth restriction (IUGR) continues to be an important determinant of perinatal mortality and morbidity in modern obstetrics [1]. Physical evidence of abnormal fetal growth becomes typically apparent in the second half of pregnancy [2], although recent studies have suggested that indicators of aberrant growth may be present as early as in the first trimester [3].

Uterine artery Doppler measurements show that impedance to flow in the urine arteries decreases with gestational age in normal pregnancies; that impedance to flow is increased in established IUGR [4]; and that this increased impedance predates the onset of the clinical syndrome of IUGR [5]. It was 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 [6]. The ductus venosus has long been discussed as being a main distributor of oxygenated blood in the fetus [7]. It is a narrow trumpet-shaped vein with an isthmic entrance, which remains narrow throughout the last half of pregnancy [8]. Since IUGR is thought to be associated with placental compromise and hypoxia, Doppler evaluation of the ductus venosus blood flow appears to be worth evaluating in the first trimester.

The aim of the work of this study was to evaluate the potentials of the first trimester (11 to 13+6 weeks) uterine artery Doppler, placental volume measurement and ductus venosus blood flow as predictors of third trimester fetal growth parameters, as well as to determine whether these measurements are independent or not in the prediction of fetal growth.

II. Methods

The current study was a prospective-observational study conducted on 200 pregnant women who attended the antenatal care clinics of El-Galaa Teaching Hospital and Al-Azhar University Hospital (SayedGalal Hospital), during a period of two years starting from June 1st 2013 till May 30th 2015.

Inclusion criteria; pregnant women with singleton pregnancy at 11 – 13+6 weeks of gestation, with a satisfactory ultrasound recording of placental volume and satisfactory Doppler recording from both uterine arteries and the ductus venosus.

Exclusion criteria;

Smoking women, pre-existing medical disorders (e.g. chronic hypertension, DM etc.), past history of preeclampsia, major fetal anomalies and IUGR.

The study purpose and procedures were explained in details and in plain terms to each of the women before required to give an informed written consent to participate in the
Hesham, First Trimester Uterine Artery Doppler, Placental Volume and Ductus Venosus Blood Flow as Predictors of Third Trimester Fetal Growth Parameters

study. Each woman were recruited for the following:

**History taking; as follows:**
- Personal history including name, age, marital status, parity, occupation, address, special habits of medical importance.
- History of the present pregnancy; focused on the risk factors associated with pregnancy as well as recognition of the inclusion and exclusion criteria.
  - Menstrual history.
  - Obstetric history.
  - Past history.
  - Family history.

**Examination; as follows:**
- General examination; blood pressure, pulse, temperature etc.
- Abdominal examination; inspection, palpation [Leopold’s maneuver] and fetal heart rate).

Ultrasound study; conducted using Voluson® E6 Expert, GE Medical system for assessment of fetal biometry for gestational age (uterine artery pulsatility index, placental volume and ductus venosus blood flow), fetal weight estimation and amniotic fluid index measurement. Gestational age was determined from the menstrual history and confirmed by the measurement of fetal crown-rump length at the first-trimester scan. A second ultrasound scan for assessment of morphology and growth parameters was arranged for the patients between 28-40 weeks of gestation, bi-parietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and femur length (FL). The examination was performed in a supine, slightly left lateral tilted position through the examination to avoid supine hypotension. Ultrasonographic and Doppler flow velocity waveforms (FVW) studies were done with pulsed-wave Doppler and real time color flow localization of the Ductus venosus and Uterine arteries.

First-trimester scan: was performed to evaluate the uterine artery PI, placental volume and the ductus venosus pulsatility index (PI) and peak velocity index for veins (PVIV). The measurements were done as follows:
- Uterine artery Doppler (Figure 1); A sagittal section of the uterus was obtained with visualization of the canal and internal cervical os. The transducer was gently tilted from side to side, and the right and left uterine arteries were identified by color flow mapping along the side of the uterine cervix at the level of the internal os. After ensuring that the angle of insonation was <50°, pulsed-wave Doppler with the sampling gate set at 2mm was used to capture the entire vessel width. The signal was updated until at least three clear similar consecutive waveforms were obtained, and the PI of the right and left uterine arteries was measured electronically once and recorded. The presence or absence of an early diastolic notch was not included in the analysis. The mean of the right and left vessels measurements was then calculated.
- Ductus venosus Doppler (Figure 2); the flow velocities from the DV were identified using color Doppler imaging in a right ventral midsagittal plane. The pulsed Doppler gate was placed in the distal portion of the umbilical sinus. Care was taken to avoid contamination from the umbilical vein, left hepatic vein, and
Hesham, First Trimester Uterine Artery Doppler, Placental Volume and Ductus Venosus Blood Flow as Predictors of Third Trimester Fetal Growth Parameters
Estimation of fetal birth weight
In order to confirm the results obtained at the third trimester scan, the study was further carried on until the time of delivery where fetal birth weight was determined. The correlation between fetal birth weight and the first trimester parameters was studied.

Data collection and statistical analysis;
The obtained anthropometric measurements were processed according to reference charts of fetal measurements set [10]. All fetal biometric parameters were converted to the gestation-specific standard score (Z-score), which was used to correct biometric measurements for differences in gestational age at the time of the ultrasound scan. The Z-score was calculated by the formula $Z=\frac{(x-\mu)}{\sigma}$ where $Z =$ Z-score, $x =$ raw value of the measure, $\mu =$ mean of the population and $\sigma =$ standard deviation (SD) the population. A Z-score of 1 and -1 indicate that the observed value is 1SD larger or smaller than the expected value, respectively.

Pearson’s correlation test was then used to study the potential relation between the first trimester parameters and the third trimester growth parameters ($Z$-BPD, $Z$-HC, $Z$-AC and $Z$-FL). The Statistical Package for Social Sciences for Windows version 12.0 (SPSS, Inc, Illinois, USA) was used for statistical analysis for all data. Numerical data were expressed as mean±SD, median and range or interquartile range. P-value < 0.05 was considered statistically significant.

A "positive correlation" is defined as a significant association of high values of one variable with high values of another. A "negative correlation" is defined as a significant association of high values of one variable with low values of another, while 'no correlation' refers to the absence of any significant association between the values of 2 variables.

The level of significance was taken at p-value <0.05, otherwise was considered statistically insignificant.
III. Results

As regards the gestational age of the studied sample, at the 1st examination the mean gestational age was 12.3 ± 1.3 weeks, with a median of 12 and an interquartile range of 11-13 weeks, 86 women were between 11-12 weeks of gestation (43%), 114 women were between 12+1-13+6 weeks of gestation (57%).

At the 2nd examination, the mean gestational age was 33.4 ± 3.7 weeks, with a median of 33 weeks and an interquartile range of 30-37 weeks of gestation. 121 women were between 28-34 weeks of gestation (60.5%), 79 women were between 35-40 weeks of gestation (39.5%) (Figure 3).
As regards the uterine artery and ductus venosus Doppler indices, the uterine artery pulsatility index was negatively correlated with all of the growth parameters, it was found that a uterine artery pulsatility index of ≥ 1.575 had a sensitivity of 79% and a specificity of 70.2% in predicting third trimester fetal growth restriction, however, the ductus venosus Doppler indices did not correlate to any of the growth parameters. (Table 1, Figures 4)

Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>BPD</th>
<th>HC</th>
<th>AC</th>
<th>FL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R</td>
<td>p</td>
<td>r</td>
<td>P</td>
</tr>
<tr>
<td>UtA PI</td>
<td>-0.55</td>
<td>0.001</td>
<td>-0.35</td>
<td>0.02</td>
</tr>
<tr>
<td>DV PI</td>
<td>-0.15</td>
<td>0.35</td>
<td>-0.13</td>
<td>0.31</td>
</tr>
<tr>
<td>DV PVIV</td>
<td>-0.12</td>
<td>0.13</td>
<td>-0.19</td>
<td>0.96</td>
</tr>
</tbody>
</table>
Hesham, First Trimester Uterine Artery Doppler, Placental Volume and Ductus Venosus Blood Flow as Predictors of Third Trimester Fetal Growth Parameters
A negative significant correlation was found between the uterine artery pulsatility index and the birth weight ($r = -0.39; p = 0.008$), however, no correlation was found between the ductus venosus and the birth weight. (Table 2 figure 5)

Table 2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Birth weight</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R</td>
<td>P</td>
</tr>
<tr>
<td>UtA PI</td>
<td>-0.39</td>
<td>0.008</td>
</tr>
<tr>
<td>DV PI</td>
<td>0.06</td>
<td>0.58</td>
</tr>
<tr>
<td>DV PVIV</td>
<td>-0.11</td>
<td>0.93</td>
</tr>
</tbody>
</table>
The significant correlation was found between the placental volume and head circumference, abdominal circumference, femur length but not with the bi-parietal diameter. However, the placental quotient was not significantly correlated with any of the parameters. (Table 3, figures 6)

**Table 3**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>BPD</th>
<th>HC</th>
<th>AC</th>
<th>FL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>p</td>
<td>r</td>
<td>p</td>
</tr>
<tr>
<td>Placental volume</td>
<td>0.18</td>
<td>0.28</td>
<td>0.53</td>
<td>0.01</td>
</tr>
<tr>
<td>Placental quotient</td>
<td>0.11</td>
<td>0.68</td>
<td>0.12</td>
<td>0.24</td>
</tr>
</tbody>
</table>
Hesham,

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

Figures 6

As regards the fetal birth weight, all of the sample were followed until delivery to confirm the obtained data, the mean fetal weight was 3175.2 ± 164.3 gm, however, no correlations were found between birth weight and both the placental volume and the placental quotient. (Table 4)

Table 4

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Birth weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Placental volume</td>
<td>0.19</td>
</tr>
<tr>
<td>Placental quotient</td>
<td>0.12</td>
</tr>
</tbody>
</table>
IV. Discussion

The small-for-gestational-age infant is often the result of a variety of maternal and fetal factors that hinder placental development. In a significant number of cases, fetal growth restriction (FGR) is associated with placental insufficiency secondary to abnormal trophoblastic invasion and subsequent defective placentation. The most common associated maternal disease is preeclampsia, in which utero placental insufficiency has been clearly demonstrated [11].

Uterine artery (UtA) Doppler velocimetry has been widely used during pregnancy to investigate the vascular downstream resistance within the placental bed and to detect failed trophoblastic invasion. Indeed, abnormal UtA Doppler velocimetry has been associated with an increased risk of developing preeclampsia or FGR in the high-risk population [12].

The current study showed that the first trimester mean uterine artery PI correlated negatively with the third trimester fetal growth parameters (BPD, HC, AC and FL) (p = 0.001, 0.02, 0.004 & 0.003 respectively), which means that higher levels of first trimester uterine artery PI was significantly associated with smaller third trimester anthropometric measurements, this correlation was further confirmed at delivery, as negative correlation was found between first trimester uterine artery PI and the birth weight (p = 0.008).

Hollis and colleagues conducted a study in 2003 [13], to determine reference values for first-trimester uterine artery resistance index (RI) in healthy pregnant women with uncomplicated pregnancies and to investigate the relationship between uterine artery Doppler indices and birth weight. It was a cross-sectional study of 265 consecutive pregnant women attending routine ultrasound examination at 11-14 weeks' gestation. Both uterine arteries were identified using color Doppler ultrasound and the RI was measured. The presence or absence of an early diastolic notch was also noted. Pregnancy outcomes were obtained from the delivery suite database and birth weight was expressed as Z-scores. The 5(th), 50(th) and 95(th) centiles for uterine artery RI between 11 and 14 weeks' gestation were 0.53, 0.71 and 0.85, respectively. Complete pregnancy outcome data were available for 246 fetuses. There was a significant negative correlation between birth-weight Z-scores and first-trimester uterine artery mean RI (r = -0.219, P = 0.001). The difference in birth weight between fetuses with absent and those with bilateral diastolic notches was also significant (P < 0.001).

Advances in 3-dimensional (3D) ultrasound technology have allowed for noninvasive measurement of the placental volume. In fact, early placental volume has been shown to be significantly associated with IUGR and preeclampsia in several studies [14].

This was a prospective cohort study including women with singleton pregnancies seen between 11 and 14 weeks as part of a screening program for aneuploidy. Placental volume and vascularization indices were obtained using 3D power Doppler imaging and...
the VOCAL technique. Placental volume (PV), Vascularization Index (VI), Flow Index (FI) and Vascularization Flow Index (VFI) were calculated. The adverse pregnancy outcomes investigated include preeclampsia (PE), gestational hypertension (GH) and small for gestational age (SGA). The predictive ability of each variable was evaluated using receiver-operating characteristic (ROC) curves. Of 388 women included, PE was seen in 30 (7.7%), GH in 37 (9.0%) and SGA in 31 (8.0%). Placental volume was not significantly different between the pregnancies with adverse outcomes and those without. The mean values of the VI and VFI were significantly lower in the pregnancies that developed PE but not in GH or SGA. The area under the ROC curve for the prediction of PE was 0.71, 0.69 and 0.70 for VI, FI and VFI, respectively.

Moreover, a previously published pilot data demonstrated how the relative contributions of both lateral placental growth and placental thickness to the placental volume may provide an enhanced assessment of early placental development and may even improve prediction of adverse pregnancy outcomes such as small-for-gestational-age (SGA) [15]. The present study found no correlation between first trimester ductus venosus pulsatility index (PI) and peak velocity index for veins (PVIV) on one hand and the third trimester growth parameters (BPD, HC, AC and FL) on the other (P = 0.35, 0.31, 0.37 and 0.51, respectively, for ductus venosus PI, and 0.13, 0.96, 0.98 and 0.71, respectively for ductus venosus PVIV). These results were confirmed at birth where again, no correlation was found between first trimester ductus venosus PI and PVIV on one hand and fetal birth weight on the other (p= 0.58 for ductus venosus PI and 0.93 for ductus venosus PVIV).

The value of first trimester ductus venosus Doppler for prediction of fetal growth abnormalities has so far seldom been studied. On the other hand, there seems to be a growing interest in the value of ductus venosus blood flow assessment at 11-14 weeks' gestation in screening for fetal chromosomal abnormalities and major fetal cardiac defects [16].

In conclusion, first trimester uterine artery Doppler can be considered a predictor of subsequent fetal growth, and women in the high-risk group may benefit from closer surveillance and possibly pharmacological preventive measure.

V. Conclusion

First trimester uterine artery Doppler can be considered a predictor of subsequent fetal growth, and women in the high-risk group may benefit from closer surveillance and possibly pharmacological preventive measure.
VI. References