Assessment of Placental Bed Vascularity and Volume in Patients with IUGR and its Correlation with Neonatal Outcome and Placental Pathology

MOSTAFA ABD EL-HAMID, M.D.*; HAZEM AL-ASHMAWY, M.D.*; AHMED ABD EL-MAGID, M.D.*; MOHAMED FAISAL, M.D.** and MOHAMED RAMADAN, M.Sc.*
The Departments of Obstetrics & Gynecology* and Pathology**, Faculty of Medicine, Cairo University

Abstract

Objectives: The aim of this study is to show the role of 3D power doppler in assessment of placental vasculature in patients with Intra Uterine Growth Retardation (IUGR) and its correlation with neonatal outcome and placental histopathology.

Study Design: Case control study.

Methodology: This study included 60 pregnant women, 30 with IUGR and 30 as control. Those patients were recruited from the Obstetric Outpatient Clinic and Obstetric Department at Kasr Al-Ainy Hospital, Faculty of Medicine, Cairo University during the period between February 2013 to August 2014. The patients were examined by 3D power doppler for placental vasculature and volume. Neonatal assessment and placental pathology were done after delivery.

Results: Placental blood perfusion in patients with IUGR is low (detected by 3D power doppler) in comparison to control group also neonatal outcome is worse with IUGR group, and placentae of IUGR group showed insufficiency.

Conclusion: 3DPD indices of placental bed vasularity revealed a significant decrease in patients with IUGR in comarison to control group.

Key Words: Three dimensional power Doppler (3DPD) – IUGR – Neonatal outcome – Placental pathology.

Introduction

INTRAUTERINE Growth Restriction (IUGR) continues to be an important determinant of perinatal mortality and morbidity in modern obstetrics [1].

The most common definition of IUGR is an estimated fetal weight at a single point in time that is below the 10th centile for gestational age [2].

Uteroplacental and fetoplacental perfusion have been extensively studied throughout gestation and after delivery. Direct investigation of the perfusion of in-vivo placentae has become possible using Three-Dimensional (3D) power Doppler sonography [3].

It did not take long to consider the possibility of a quantitative vascular analysis of the region observed. This was analyzed through the vascular indices as VI (vascularization index), FI (flow index) and VFI (vascularization flow index), which show the quantity of vessels, the local blood flow and their combination [4].

The pre-determined area was formed of small pieces of volume named voxels. From then on, they were divided into gray voxels, pieces that compose the noncolored part of the three-dimensional area with black and white tones, and colored voxels, formed by the colored part of this section, both measured in a scale of 0-100 [5].

The VI is the index of the number of colored voxels that have been studied before and showed, indirectly, the number of vessels contained. The movement of the blood in the vessels was showed with spring colors, while the FI was an average of the intensity of the colors from the voxels, in other words, the intensity of the blood flow. The VFI, however, is the average of the intensity of all kinds of voxels [6].

Nowadays, all these indices can be calculated in a pre-determined area, automatically or not, through a program that is followed in a series of three-dimensional ultrasound machines named VOCAL (virtual organ computer-aided analysis) [3].
The placenta is a fetal organ with important metabolic, endocrine and immunologic functions besides being responsible for nutrition, respiration and excretion for the fetus. Lastly acting as a barrier, it has a role in protecting the fetus from noxious agents (Holland and Brews, 1998). Placental formation begins in the latter half of the 2nd month of pregnancy and is usually completed by the 4th months. It reaches its maximum growth at term [7].

Endovascular trophoblast normally invades the spiral arteries of the uterus and converts them into uteroplacental arteries. This takes place in two stages. In the first and early second trimester, only the decidual part of the spiral arteries is converted. The so-called second wave of invasion occurs in the middle of the second trimester, and converts the myometrial part of the spiral arteries to create a low-resistance circulation which allows high blood flow to the placenta. In many pregnancies complicated by growth restriction and preeclampsia, this second wave of trophoblast invasion fails [8].

A useful clinical tool to identify those neonates who require resuscitation as well as to assess the effectiveness of any resuscitative measures is the Apgar scoring system [9].

Each of the five easily identifiable characteristics-heart rate, respiratory effort, muscle tone, reflex irritability, and color is assessed and assigned a value of 0 to 2. The total score, based on the sum of the five components, is determined 1 and 5 minutes after delivery.

The 1-minute Apgar score reflects need for immediate resuscitation.

The 5-minute score, and particularly the change in score between 1 and 5 minutes, is a useful index of the effectiveness of resuscitative efforts. The 5-minute Apgar score also has prognostic significance for neonatal survival, because survival is related closely to the condition of the infant in the delivery room [9].

Aim of the work:

The aim of this study is to show the value of 3D power doppler in assessment of placental vasculature in patients with IUGR and its correlation with neonatal outcome and placental histopathology.

Patients and Methods

This study is a case control study which included 60 pregnant women, 30 with IUGR and 30 control. Those patients were recruited from the obstetric outpatient clinic and obstetric department at Kasr Al-Ainy Hospital, Faculty of Medicine, Cairo University during the period between February 2013 to August 2014.

Case criteria:

Age (18-45) years, singleton viable pregnancy, gestational from 28 to 40 weeks, normal fetal anatomy, visualized totally anterior wall placenta, patients with fetal weight below 10th percentile on growth charts.

Control criteria:

The same criteria but fetal weight between 10th and 90th percentile on growth charts.

Interventions:

During pregnancy:

All these pregnant women were subjected to history, clinical examination, laboratory investigations and ultrasound examinations.

Ultrasound examination:

Ultrasound examinations were performed using Voluson E8 Expert (General Electric Medical Systems) with a volumetric abdominal probe RAB 4-8D (4-8 MHz). Ultrasound examinations were done every 2 to 3 weeks. Ultrasound examinations were performed by a single operator.

Two dimensional ultrasound: It was used for (gestational age, fetal weight, and placental site).

Three dimensional ultrasound and power doppler (3D U/S, 3D power doppler):

It is done for evaluation placental volume and vascular indices Vascularization Index (VI), Flow Index (FI) and Vascularization Flow Index (VFI) with the use of 3D Power Doppler and VOCAL technique.

After delivery:

I- Newborn:

The newborns were evaluated after delivery by:

1- Apgar score at 5th minutes (according to our results we had 2 groups of neonates, normal apgar score ≥ 7, low apgar score <7.2. Birth weight.

II- Placenta:

All sections were examined by the same pathologist without knowledge of the clinical history and blood flow results.
The placentae were examined for the following:
A- Grossly (weight, infarcts, calcifications and degenerations).
B- Microscopically (villous hypermaturity, ischemia, presence of avascular villi, massive perivillous fibrin deposition, and vessel wall thickening [10].

Statistical analysis:
Results are expressed as mean ± standard deviation or number (%). Comparison between numerical data in three studied groups was performed using one way ANOVA followed by LSD test if significant results were recorded. Comparison between categorical data was performed using Chi square test. Correlation between different variable was performed using Pearson correlation coefficient test. SPSS computer program (version 16 windows) was used for data analysis. p-value less than or equal to 0.05 was considered significant and less than 0.01 was considered highly significant.

Results
The current study was a case control study, which included 60 pregnant women, 30 with IUGR (Group 1) and 30 control (Group 2). Those patients were recruited from the obstetric outpatient clinic and obstetric department at Kasr Al-Ainy Hospital, Faculty of Medicine, Cairo University during the period between February 2013 to August 2014.

Table (1): Demographic features of the two studied groups.

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (N=30)</th>
<th>Group 2 (N=30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs.)</td>
<td>27.02±4.71</td>
<td>26.64±5.46</td>
<td>0.750 (NS)</td>
</tr>
<tr>
<td>Parity</td>
<td>2.26±1.26</td>
<td>2.08±1.08</td>
<td>0.079 (NS)</td>
</tr>
<tr>
<td>Gestational Age (GA)</td>
<td>33.96±1.38</td>
<td>38.1±2.68</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD. NS=p>0.05=Not significant. a p<0.01=Highly significant.

There was no statistical significant difference (p>0.05) between the two groups as regard age, and parity but there was highly significant difference between them in relation to gestational age at termination.

Table (2): Comparison between mean values of placental vascular indices (VI, VFI and FI) in the two groups.

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (30 patients)</th>
<th>Group 2 (30 patients)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VI</td>
<td>10.01±4.91</td>
<td>18.04±4.38</td>
<td>0.001</td>
</tr>
<tr>
<td>VFI</td>
<td>5.20±3.55</td>
<td>10.16±2.62</td>
<td>0.001</td>
</tr>
<tr>
<td>FI</td>
<td>19.96±5.54</td>
<td>32.56±4.78</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD. a p<0.01=Highly significant.

Patients in Group 1 showed low VI, VFI, FI in comparison to Group 2 with statistically highly significant difference.

Table (3): Correlation between placental volume and weight and placental vascular indices (VI, VFI, FI) in the studied patients.

<table>
<thead>
<tr>
<th></th>
<th>Placental volume</th>
<th>Placental weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>p-value</td>
</tr>
<tr>
<td>VI</td>
<td>0.726</td>
<td>0.001**</td>
</tr>
<tr>
<td>VFI</td>
<td>0.595</td>
<td>0.001**</td>
</tr>
<tr>
<td>FI</td>
<td>0.762</td>
<td>0.001**</td>
</tr>
</tbody>
</table>

r : Pearson Correlation.
**: p<0.01=Correlation is significant at the 0.01 level (2-tailed).

There was statistical significant (p<0.05) direct correlation between placental volume (detected by 3D U/S) and placental weight (detected after delivery) versus placental vascular indices (VI, VFI, FI).

Table (4): Relation between mean values of placental vascular indices parameters (VI, VFI & FI) and the mode of delivery.

<table>
<thead>
<tr>
<th></th>
<th>Normal (N=25)</th>
<th>CS (N=35)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VI</td>
<td>16.79±6.32</td>
<td>11.94±6.09</td>
<td>0.001**</td>
</tr>
<tr>
<td>VFI</td>
<td>9.76±6.92</td>
<td>4.80±3.02</td>
<td>0.001**</td>
</tr>
<tr>
<td>FI</td>
<td>31.44±9.00</td>
<td>24.20±7.38</td>
<td>0.001**</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD.
**: p<0.01=Highly significant.

There was statistical significant difference (p<0.05) between vascular indices in the patients according to mode of delivery, the lower the indices the higher the incidence of CS.

Table (5): Relation between mean values of placental vascular indices parameters (VI, VFI & FI) and placental histopathology in the studied patients.

<table>
<thead>
<tr>
<th></th>
<th>Normal (N=23)</th>
<th>Insufficiency (N=37)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VI</td>
<td>18.8±5.36</td>
<td>9.84±4.34</td>
<td>0.001**</td>
</tr>
<tr>
<td>VFI</td>
<td>10.23±6.48</td>
<td>4.32±3.12</td>
<td>0.001**</td>
</tr>
<tr>
<td>FI</td>
<td>33.42±7.85</td>
<td>22.22±6.04</td>
<td>0.001**</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD. **: p<0.01=Highly significant.

There was statistical significant difference (p<0.05) between vascular indices in the patients according to placental histopathology, the lower the indices the higher the incidence of placental insufficiency.
Table (6): Relation between mean values of placental vascular indices parameters (VI, VFI & FI) and the apgar score in the studied patients.

<table>
<thead>
<tr>
<th>Apgar score</th>
<th>Normal (n=45)</th>
<th>Low (n=15)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placental vascular indices</td>
<td>Appar score ≥7 at 5 minutes</td>
<td>Appar score &lt;7 at 5 minutes</td>
<td></td>
</tr>
<tr>
<td>VI</td>
<td>17.03±6.25</td>
<td>10.25±4.88</td>
<td>0.001**</td>
</tr>
<tr>
<td>VFI</td>
<td>8.95±6.51</td>
<td>4.77±3.56</td>
<td>0.001**</td>
</tr>
<tr>
<td>FI</td>
<td>31.07±8.61</td>
<td>22.95±7.14</td>
<td>0.001**</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD.

**: p<0.01=Highly significant.

There was statistical significant difference (p<0.05) between vascular indices in the patients according to the apgar score of the neonates, the lower the indices the higher the incidence of a neonate with low apgar.

Table (7): Correlation between birth weight and placental vascular indices (VI, VFI, FI) in the studied patients.

<table>
<thead>
<tr>
<th>Birth weight</th>
<th>r</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VI</td>
<td>0.698</td>
<td>0.001**</td>
</tr>
<tr>
<td>VFI</td>
<td>0.550</td>
<td>0.001**</td>
</tr>
<tr>
<td>FI</td>
<td>0.782</td>
<td>0.001**</td>
</tr>
</tbody>
</table>

r : Pearson Correlation.

**: p<0.01=Correlation is significant at the 0.01 level (2-tailed).

There was statistical significant (p<0.05) direct correlation between neonatal birth weight versus placental vascular indices (VI, VFI, FI), this means the low the placental vascular indices, the low the neonatal birth weight.

Discussion

The present study showed that no statistical significant difference (p>0.05) between patients as regard age, and parity but there was significant difference (p<0.05) between patients with IUGR affection (Group 1) and control group (Group 2), as regards gestational age at termination, this indicates that vascularity affection was reflected on fetal wellbeing ending by termination of pregnancy.

Our study showed that patients in group (patients with IUGR) showed low VI, FI, VFI (statistically high significant difference) (p<0.001) in comparison to patients in Group 1 (control group).

The changes of placental vascularity was detected by placental vascular indices (VI, VFI, FI) earlier than reflection on fetal doppler indices.

This may give us a chance to use drugs that improve placental circulation, delay the onset of the disease and prevent the progression of the disease.

Guiot et al., performed a study on a group of 45 pregnant women between 23 and 37 weeks of gestation, including 30 IUGR and 15 normal pregnancies. Placental vascular indices were calculated for five different regions of the placenta. The authors stated that VI, FI, and VFI values were significantly lower in the IUGR pregnancies [11].

Michal Pomorski et al., published a prospective study included 120 pregnant patients, the normal pregnancy group included 100 patients and the IUGR pregnancy group included 20 patients, placental vasculature in normal and IUGR pregnancies were compared, the values of VI, FI, and VFI are statistically significantly lower in the IUGR group compared to those in the normal group [12].

In the present study there was statistical significant (p<0.05) direct correlation between placental volume (detected by 3D U/S) and placental weight (detected after delivery) versus placental vascular indices (VI, VFI, FI).

Michal Pomorski et al., 2012, showed that there was statistically important differences of placental volume between the normal pregnancy and the IUGR pregnancy groups, and this finding was directly correlated with placental vascular indices [12].

In the present study we found that patients with low placental vascular were delivered mainly by cesarean section, this was done to prevent excessive fetal hypoxia that may occur due to passage through normal delivery.

Riskin et al., showed that the optimal mode of delivery for women at high risk of delivering a small baby is controversial.

In the present study we found that patients with low placental vascular indices had worse neonatal outcome.

The present study showed high significant value (p<0.001) direct correlation between placental vascular indices (VI, VFI, and FI) and neonatal birth weight, the lower the indices the lower birth weight.

According to these data we can further make a linear regression curve to make an equation between the indices and birth weight which will help us to predict birth weight by using these...
Mostafa Abd El-Hamid, et al. 1355

indices. To the best of our knowledge we did not find any researches that cover this point as regards correlation.

In the present study we found that patients with low placental vascular indices had placental insufficiency in comparison to patients with normal indices.

Histological abnormalities such as the presence of villous fibrinoid necrosis, villous hypermaturity, and placental infarction were observed significantly more often in the hypertensive placentas [13].

Placental infarctions are the most common placental lesions, and their presence is a continuum from normal changes to extensive and pathological involvement. If they are numerous, thick, centrally located, and randomly distributed, placental insufficiency may develop [14].

Conclusion:

Placental vascular indices (VI, FI, and VFI) are early predictors of placental hypoperfusion and ischemia, placental vascular indices (VI, FI, and VFI) are good predictors of pregnancy outcome (neonatal outcome, placental volume and weight). According to the high correlation between the placental vascular indices and birth weight, we can make an equation to predict expected fetal weight.

References


تعتبر موجات الدوائر الثلاثية للأبعاد من أهم الوسائط المستخدمة في الكشف عن التغيرات غير الطبيعية التي تحدث بالأوعية الدموية المشوية.

وقد تم اجراء هذه الدراسة في مستشفى أمراض النساء والتوليد بجامعة القاهرة حيث اشتملت هذه الدراسة على ستون سيدة من الحوامل منهم ثلاثون يعانين من نمو الاجنة. وقد أجريت هذه الدراسة لبحث ما إذا كان الدوائر الثلاثية للأبعاد قادر على تقييم الأوعية الدموية المشوية في مرضى تأخر نمو الاجنة وعلاقة مع نتائج التحليل البانولوجي للمشيمة والحالة الصحية لحديدي الولادة. تم أخذ التاريخ المرضي وإجراء فحص أكينتيكي شامل والفحوصات العملية اللازمة وموجات فوق صوتية ثنائية وثلاثية للأبعاد خاصة على المشيمة وبعد الولادة تم تقييم حديثي الولادة وارسال المشيمة للتحليل البانولوجي.

وقد تم جمع المعلومات وتحليل النتائج وعمل دراسة إحصائية طبقاً للقواعد الإحصائية المناسبة حيث استُرفت الدراسة عن الآتي:

١- السيدات الحوامل بالمراحل المتقدمة يعانين من نقص الدم المتطرف للمشيمة (VFI)، متوسط معدل سریان الدم (FI) ومتوسط معدل سریان الدم الوعائي (VfI) بالمقارنة بالحوامل اللائي لا يعانين من نقص حجم ووزن المشيمة.

٢- السيدات الحوامل اللائي يعانيين من نقص الدم المتطرف للمشيمة يعانيين من نقص حجم ووزن المشيمة.

٣- وجود علاقة إحصائية طردية بين معدلات الموجات فوق صوتية ثلاثية الأبعاد وحجم ووزن المشيمة.

٤- المرضى اللائي يعانيين من معدلات الموجات فوق صوتية ثلاثية الأبعاد المنخفضة تحت ولادتهم غالباً عن طريق الولادة القصرية.

٥- المرضى اللائي يعانيين من معدلات الموجات فوق صوتية ثلاثية الأبعاد المنخفضة كانت مواليدهم أسوأً طبقاً لتقييم أبجر، كما توجد علاقة إحصائية طردية بين معدلات الموجات فوق صوتية ثلاثية الأبعاد ووزن حديثي الولادة.

٦- المرضى اللائي يعانيين من معدلات الموجات فوق صوتية ثلاثية الأبعاد المنخفضة يعانيين أيضاً من قصور في السريان الوعائي للمشيمة.

استناداً إلى التحليل البانولوجي للمشيمة.