Study of Intraplacental Vascularization by 3D Power Doppler Ultrasound in Pregnancies with Normal Evolution

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Abstract

Introduction. *Human placenta represents an interface between two distinct circulations, maternal and fetal circulations. The complex physiological mechanisms of transfer between the 2 components are still a controversial area, under the focus of researchers. Nowadays ultrasound evaluation of the placenta is extremely important.* ***Objectives****. The aim of this study was to evaluate the development of intraplacental vascularization by the determination of intraplacental vascularization indices during the course of pregnancies with normal evolution. Material and method. The study included 80 pregnant women aged between 23 and 37 years, assessed in the period 1 June 2009 - 31 May 2010. The two-dimensional, three-dimensional and Doppler ultrasound examinations were performed with an ACCUVIX V10 ultrasound machine, equipped with a 3.5 MHz probe.* ***Results.*** *RI decreased proportionally and progressively during the course of pregnancy (Pearson correlation coefficient r=-0.704; P<0.000). For the accuracy of the interpretation of this relation, the fact that gestational age was analyzed only at 5 time points (14, 22, 28, 32, and 38 weeks) was also considered and an analysis of the Spearman correlation coefficient showed that RI decreased directly proportionally to gestational age (-0.754; P<0.000). For the other parameters, no significant global correlations with gestational age were described. A tendency to linear dependence between FI and VI, as well as between FI and VFI, was evidenced. There was a statistically significant direct proportionality relation between VI and VFI. No parameter was correlated with RI if all gestational ages were taken into account. A tendency to obtain a correlation between between RI, FI, VI and VFI was found, particularly at 14 and 28 weeks.* ***Conclusions.*** *The correlation of placental vascularization indices with other ultrasound parameters is an aim in researchers attention*
Keywords: *placenta, 3D power Doppler ultrasound, vascularization indices*

Introduction

Human placenta represents an interface between two distinct circulations, maternal and fetal circulations. The complex physiological mechanisms of transfer between the 2 components are still a controversial area, under the focus of researchers. Placental vascularization is an essential component in the normal evolution of pregnancy[1,2]. An inadequate development of the placenta may result in intrauterine growth retardation, fetal hypoxia, preeclampsia, premature birth. The assessment of the intrauterine fetal status is a permanent concern of modern obstetrics[3,4,5]. In this context a particular attention is given to ultrasound evaluation of placenta[6,7,8]. 3D ultrasound combined with power Doppler has to become a routine procedure in monitoring of pregnancy[9,10,11]. This is going to be used at different gestational ages in order to asess the development of placental vascularization[12,13].

The aim of this study is to evaluate the development of intraplacental vascularization by the determination of intraplacental vascularization indices during the course of pregnancies with normal evolution.

Material and method

The study included 80 pregnant women aged between 23 and 37 years, assessed in the period 1 June 2009 - 31 May 2010.

The ultrasound examination was performed between 14 WA and 38 WA. The pregnant women were included in the study during the first 8 weeks of pregnancy. Their consent for the ultrasound evaluation of pregnancy at fixed time intervals was obtained.

The patients having a history of pregnancy associated with vascular pathology were excluded from the study. Twelve pregnancies that developed vascular pathology during the course of evolution were also excluded from the study. Patients with arterial hypertension, diabetes mellitus or other cardiovascular diseases were not included in the study.

Two-dimensional, three-dimensional and Doppler ultrasound examinations were performed with an ACCUVIX V10 ultrasound machine, equipped with a 3.5 MHz probe.

The ultrasound evaluation started with two-dimensional ultrasound, which assessed the location and thickness of placental tissue, as well as the placental structure. The normal evolution of the two-dimensional ultrasound aspect was assessed using the placental maturity grading defined by Grannum.

Then, Doppler ultrasound was performed, with the determination of the resistivity index (RI) at the level of the umbilical arteries. The evolution of this parameter was assessed by reference to Le Maout's diagram.

The next stage was the qualitative evaluation of intraplacental vascularization, by the performance of power Doppler ultrasound, which allowed to evidence the intraplacental blood flow. During the course of pregnancy, the number of intraplacental vessels evidenced by this examination technique was monitored.

Subsequently, 3D power Doppler ultrasound was performed. The association of 3D ultrasound with power Doppler exploration provided additional information, by evidencing the vascular pattern of the placenta. In the first trimester of pregnancy, the whole placental volume was visualized, but the separation of placental from non-placental vascularization was difficult. In the second and third trimesters of pregnancy, the visualization of the whole placenta was not possible. As a result, we performed ultrasound examination during the second and third trimesters of pregnancy using the method of "placental vascular biopsy" described by Luis T. Mercé et al. This technique involves the acquisition of the 3D image by means of the VOCAL software, using the spherical mode. After the estimation of the placental volume, the histogram was used for the determination of vascular indices. The VOCAL software automatically calculates the 3 vascularization and flow indices at placental level: VI is the vascularization index, which determines the percentage of color in the volume of interest, so it is the representation of blood vessels in the explored territory. FI is the flow index, being the expression of blood flow intensity. VFI is defined as a vascularization flow index and assesses both vascularization and blood flow.

Statistical processing (Student, ANOVA, Pearson tests) was performed using the SPSS application. Descriptive statistics and graphic representation used the Microsoft Excel 2003 application.

Results

Placental volume significantly increased with the evolution of pregnancy.

During the course of pregnancy, dynamic changes in the appearance of the placenta were noted, according to the placental maturity grades described by Grannum (Figure 1 and Figure 2).

Power Doppler ultrasound was used for the analysis of the presence of the blood flow. As pregnancy progressed, an increase in the number of intraplacental vascular branches was evidenced (Figure 3).

3D power Doppler allowed to visualize the vascular tree, including the arteries from third order stem villi, structures that cannot be evidenced with certainty by the other ultrasound techniques (Figure 4).

For all pregnancies included in the study, placental resistivity was assessed by the measurement of the resistivity index (RI) at the level of the umbilical artery (Figure 5). The values of this index were correlated with the three intraplacental vascularization indices. RI decreased proportionally and progressively during the course of pregnancy (Pearson correlation coefficient r=-0.704; P<0.000). For the accuracy of the interpretation of this relation, the fact that gestational age was analyzed only at 5 time points (14, 22, 28, 32, and 38 weeks) was also considered and the analysis of the Spearman correlation coefficient showed that RI decreased directly proportionally to gestational age (-0.754; P<0.000) (Figure 6).

For the other parameters, no significant global correlations with gestational age were described: VI (Pearson correlation coefficient r=-0.261; P<0.001 and Spearman coefficient -0.388; P<0.000) and VFI (Pearson correlation coefficient r=-0.194; P<0.017 and Spearman coefficient -0.200; P<0.014) had a tendency to correlate with gestational age, while FI (Pearson correlation coefficient r=-0.045; P<0.584 and Spearman coefficient -0.50; P<0.545) did not correlate with gestational age (Figure 7, Figure 8 and Figure 9).

The comparative analysis of the proportionality relation between the four parameters is shown in Table 1.

As it can be seen, a tendency to a linear dependence between FI and VI, as well as between FI and VFI, was evidenced. There was a statistically significant direct proportionality relation between VI and VFI. No parameter was correlated with RI if all gestational ages were taken into account (Figure 10, Figure 11 and Figure 12).

The stratified comparative analysis of the proportionality relation between the four parameters is shown in Tables 2-6.

These results show a tendency to obtain a correlation between the parameters, particularly for weeks 14 and 28.

Discussion

The actual study has attempted the correlation of placental vascularization indices with gestational age, as well as the placental volume and resistivity index determined at the levelof the umbilical artery. We have evaluated the distribution

Figure 1. Two-dimensional ultrasound 14 WA

Figure 2. Two-dimensional ultrasound 22 WA

Figure 3. Power Doppler ultrasound 28 WA - intraplacental circulation

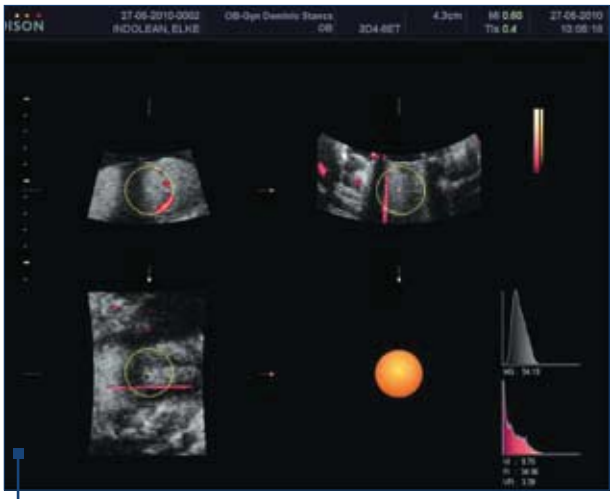

Figure 4. 3D power Doppler ultrasound - 28 WA

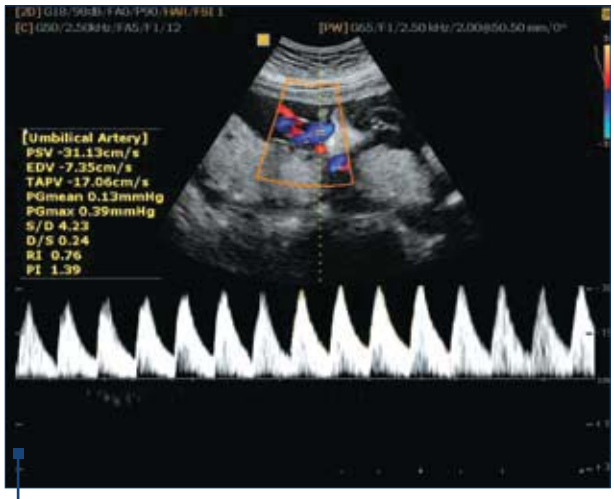

Figure 5. Umbilical artery 28 WA - normal RI

of those indices using Pearson correlation coefficient, as well as the Spearman coefficient. Reviewing the results to the literature updates has been difficult, because of the diversity of the statistical methods used by different authors. Recent studies recommend the evaluation of the distribution of indices by regression, the histogram analysis, and the Shapiro-Wilk and Kolmogorov-Smirrnov tests. The Pearson correlation test can be used in order to assess the correlation between placental indices and gestational age, placental volume, respectively. Other authors recommend the ANOVA tests or the SPSS software recomanded[5,6,13].

About the correlation of placental vascularization indices with gestational age in our study, we found the maintenance of FI values, while VI and VFI had a slight increase until 32 WA, after which they were maintained at plateau values or decreased slightly. Consequently, the 2 indices, VI and VFI, could be correlated with gestational age. These results are sustained by studies that report a similar evolution of VI and VFI,

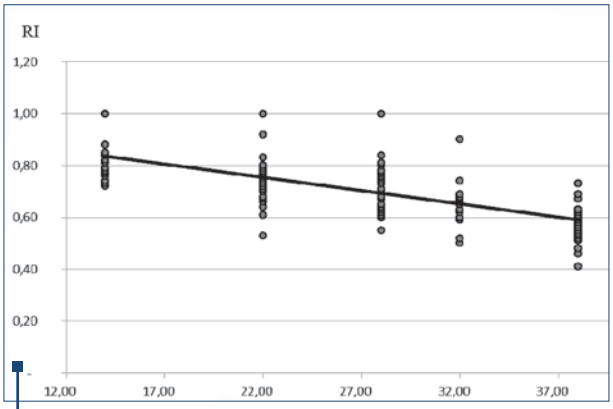

Figure 6. Correlation between gestational age and RI

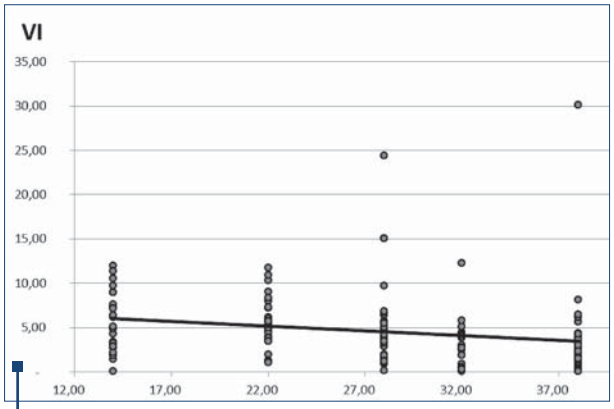

Figure 7. Correlation between gestational age and VI

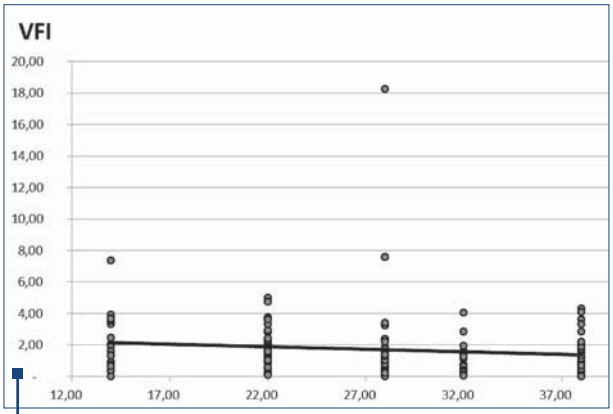

Figure 8. Correlation between gestational age and VFI

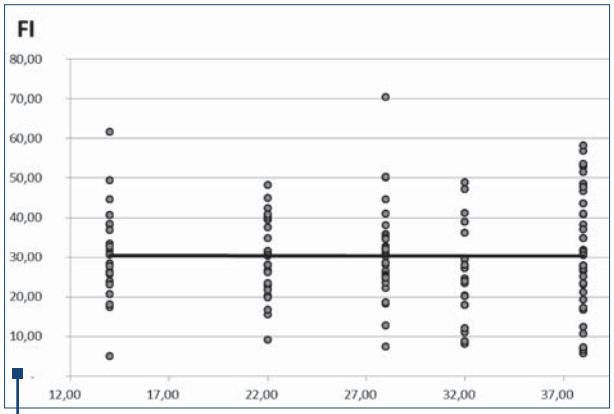

Figure 9. Correlation between gestational age and FI

Table 1 Correlations between the parameters for all gestational ages

		RI	VI	FI	VFI
RI	Pearson correlation coefficient	1.000	0.116	-0.081	0.035
	P		0.162	0.332	0.674
VI	Pearson correlation coefficient	0.116	1.000	0.494	0.830
	P	0.162		0.000	0.000
FI	Pearson correlation coefficient	-0.081	0.494	1.000	0.678
	P	0.332	0.000		0.000
VFI	Pearson correlation coefficient	0.035	0.830	0.678	1.000
	P	0.674	0.000	0.000	

while for FI the evolution is different, meaning an increase of the pregnancy evolution, other authors describe a constant menteinance of all 3 indices during the pregnancy[6,7,8,13,14,15]. We consider that these differences can be determined by different methods of harvesting the placental samples. We found a tendency to a linear dependence between FI and VI, as well as between FI and VFI. There is a statistically significant direct proportionality relation between VI and VFI.

In the studied pregnancies the placental volum and the placental vascularization indices has not been influenced by the mother`s age, a fact proved by the literature studies[6,8,13].

We consider that the determination of the development methods of the 3 indices of vascularization in normal pregnancies is importantbeing a reference part in the surveilance of the pregnancies that will develop vascular pathology[10,16,17].

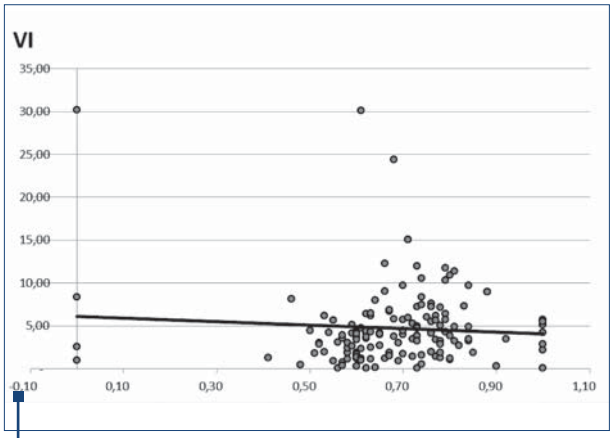

Figure 10. Correlation between RI and VI

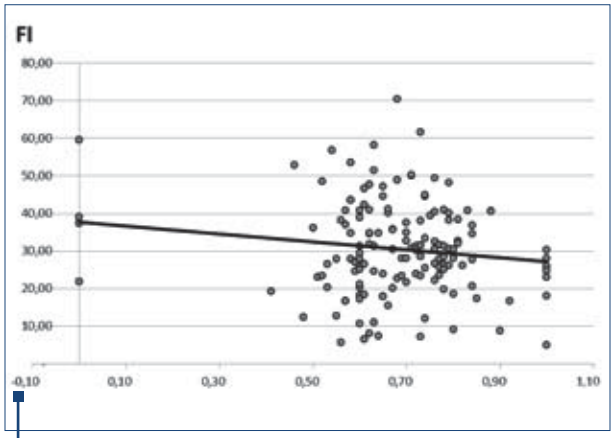

Figure 11. Correlation between RI and FI

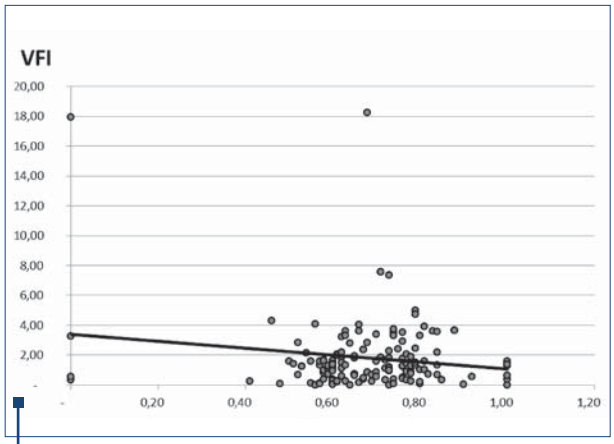

Figure 12. Correlation between RI and VFI

Another objective of the study has been the correlation of the placental vascularization indices with placental volume. We have remarked an increase of the values of those indices while the placental volume has increased. Actual studies are even in this way various. Some authors say that the placental vascularization increase depending of its volume, while other studies report a decrease of those indices when placental volume increase[18,19].

The third objective of the study has been represented by the correlation of placental vascularization indices with umbilical RI. In our study, the RI values were significantly correlated with intraplacental vascularization indices at 14 and 28 weeks of pregnancy. We consider this aspect extremely important because it is known that big values of the umbilical RI appear when 70% of placental vessels are affected[1,20]. Considering those, the meassure of vascula-

Table 2 Relations between the parameters for 14 weeks

		RI	VI	FI	VFI
RI	Pearson correlation coefficient	1.000	-0.387	-0.543	-0.409
	P		0.062	0.006	0.047
	Case number	24	24	24	24
VI	Pearson correlation coefficient	-0.387	1.000	0.783	0.977
	P	0.062		0.000	0.000
	Case number	24	26	26	26
FI	Pearson correlation coefficient	-0.543	0.783	1.000	0.774
	P	0.006	0.000		0.000
	Case number	24	26	26	26
VFI	Pearson correlation coefficient	-0.409	0.977	0.774	1.000
	P	0.047	0.000	0.000	
	Case number	24	26	26	26

Table 3 Relations between the parameters for 22 weeks

		RI	VI	FI	VFI
RI	Pearson correlation coefficient	1.000	0.028	-0.068	0.042
	P		0.884	0.722	0.827
	Case number	31	30	30	30
VI	Pearson correlation coefficient	0.028	1.000	0.704	0.937
	P	0.884		0.000	0.000
	Case number	30	30	30	30
FI	Pearson correlation coefficient	-0.068	0.704	1.000	0.846
	P	0.722	0.000		0.000
	Case number	30	30	30	30
VFI	Pearson correlation coefficient	0.042	0.937	0.846	1.000
	P	0.827	0.000	0.000	
	Case number	30	30	30	30

Table 4 Relations between the parameters for 28 weeks

		RI	VI	FI	VFI
RI	Pearson correlation coefficient	1.000	0.013	0.072	-0.045
	P		0.942	0.679	0.799
	Case number	36	35	35	35
VI	Pearson correlation coefficient	0.013	1.000	0.843	0.959
	P	0.942		0.000	0.000
	Case number	35	35	35	35
FI	Pearson correlation coefficient	0.072	0.843	1.000	0.833
	P	0.679	0.000		0.000
	Case number	35	35	35	35
VFI	Pearson correlation coefficient	-0.045	0.959	0.833	1.000
	P	0.799	0.000	0.000	
	Case number	35	35	35	35

Table 5 Relations between the parameters for 32 weeks

		RI	VI	FI	VFI
RI	Pearson correlation coefficient	1.000	-0.268	-0.306	-0.212
	P		0.268	0.202	0.384
	Case number	19	19	19	19
VI	Pearson correlation coefficient	-0.268	1.000	0.575	0.913
	P	0.268		0.008	0.000
	Case number	19	20	20	20
FI	Pearson correlation coefficient	-0.306	0.575	1.000	0.742
	P	0.202	0.008		0.000
	Case number	19	20	20	20
VFI	Pearson correlation coefficient	-0.212	0.913	0.742	1.000
	P	0.384	0.000	0.000	
	Case number	19	20	20	20

Table 6 Relations between the parameters for 38 weeks

		RI	VI	FI	VFI
RI	Pearson correlation coefficient	1.000	0.059	-0.049	-0.118
	P		0.724	0.771	0.481
	Case number	38	38	38	38
VI	Pearson correlation coefficient	0.059	1.000	0.006	0.386
	P	0.724		0.971	0.015
	Case number	38	39	39	39
FI	Pearson correlation coefficient	-0.049	0.006	1.000	0.716
	P	0.771	0.971		0.000
	Case number	38	39	39	39
VFI	Pearson correlation coefficient	-0.118	0.386	0.716	1.000
	P	0.481	0.015	0.000	
	Case number	38	39	39	39

rization and flow indices might allow an early detection of intrauterine fetal growth disorders and chronic fetal distress.

In the ultimate years studies it is put an important emphasis of the aspect of the placenta, which concernes the evaluation of the intrauterine fetal status, because the placenta influences the development of the product of conception with its major role in feto-maternal exchanges[13,19,20].

Conclusions

3D power Doppler ultrasound allows the study of placental vascularization.

The correlation of placental vascularization indices with other ultrasound parameters is an important aim, in the researchers attention.

The 3D power Doppler ultrasound examination by the method of "placental vascular biopsy" is an effective technique for the evaluation of placental vascularization during the course of pregnancy.

VI and VFI could be correlated with gestational age. There is a statistically significant direct proportionality relation between VI and VFI.

RI values were significantly correlated with intraplacental vascularization indices at 14 and 28 weeks of pregnancy. ■

References

1. Mihu D., Ecografia Doppler în obstetrică şi ginecologie. Cluj-Napoca: Editura Clusium; 2001.
2. Rizzo G., Capponi A., Cavicchioni O., Vendola M., Arduini D., Placental vascularization measured by three-dimensional power Doppler ultrasound at 11 to 13 + 6 weeks' gestation in normal and aneuploid fetuses. Ultrasound Obstet Gynecol. 2008; 31(1):111-2.
3. Bozkurt N., Başgül Yigiter A., Gokaslan H., Kavak Z.N., Correlations of fetal-maternal outcomes and first trimester 3-D placental volume/3-D power Doppler calculations. Clin Exp Obstet Gynecol. 2010; 37(1): 26-8.
4. Rizzo G., Capponi A., Pietrolucci M.E., Capece A., Arduini D., First-trimester placental volume and vascularization measured by 3-dimensional power Doppler sonography in pregnancies with low serum pregnancy-associated plasma protein a levels.. J Ultrasound Med. 2009 Dec; 28(12): 1615-22.
5. Noguchi J., Hata K., Tanaka H., Hata T., Placental vascular sonobiopsy using three-dimensional power Doppler ultrasound in normal and growth restricted fetuses. Placenta. 2009 May; 30(5): 391-7.
6. C.F.S. de Paula, R. Ruano, J.A.D.B. Campos, M. Zugaib, Quantitative Analysis of Placental Vasculature by Three-Dimensional Power Doppler Ultrasonography in Normal Pregnancies From 12 to 40 Weeks of Gestation. Placenta.2009; 30(2): 142-148.
7. J.S. Abramowicz, E. Sheiner. Ultrasound of the Placenta: A Systematic Approach. Part I: Imaging. Placenta. 2008; 29(3): 225-240.
8. J.S. Abramowicz, E. Sheiner. Ultrasound of the Placenta: A Systematic Approach. Part II: Functional Assessment(Doppler). Placenta. 2008; 29: 921-929.
9. Schulten-Wijman M.J., Struijk P.C., Brezinka C., De Jong N., Steegers E.A., Evaluation of volume vascularization index and flow index: a phantom study. Ultrasound Obstet Gynecol. 2008 Sep; 32(4): 560-4.
10. Guiot C., Gaglioti P., Oberto M., Piccoli E., Rosato R., Todros T., Is three-dimensional power Doppler ultrasound useful in the assessment of placental perfusion in normal and growth-restricted pregnancies? Ultrasound Obstet Gynecol. 2008 Feb; 31(2): 171-6.
11. Ivica Zalud, Steven Shaha. Evaluation of the utero-placental circulation by three-dimensional Doppler ultrasound in the second trimester of normal pregnancy. Journal of Maternal-Fetal & Neonatal Medicine. 2007; 20(4): 299-305.
12. Rizzo G., Capponi A., Cavicchioni O., Vendola M., Arduini D., Placental vascularization measured by three-dimensional power Doppler ultrasound at 11 to 13 + 6 weeks' gestation in normal and aneuploid fetuses. Ultrasound Obstet Gynecol. 2007; 30(3): 259-62.
13. Luis T. Mercé, Maria J. Barco, Santiago Bau, Sanja Kupešić, Asim Kurjak. Assessment of Placental Vascularization by Three- Dimensuional Power Doppler "Vascular Biopsy" in Normal Pregnancies. Croat Med J 2005; 46(5): 765-771.
14. Hélio Antonio Guimarães Füho, Lavoisier Linhares Dias du Costa, Edward Araújo Junior, Luciano Marcondes Machado Nardozza, Paulo Martin Nowak, Antonio Fernandes Morou, Rosiane Mattar, Cláudio Rodrigues Pires. Placenta: angiogenesis and vascular assessment throught three- dimensional power Doppler ultrasonography. Arch Gynecol Obstet. 2008. 277: 195-200.
15. Partleitner H., Steiner H., Hasenoehrl G., Staudach A., Threee-dimensional power Doppler sonography: imaging and quantifying blood flow and vascularization. Ultrasound Obstet. Gynecol. 1999;14:139-143.
16. Ivica Zalud, Steven Shaha. Three-dimensional sonography of the placental and uterine spiral vasculature: Influence of maternal age and parity. 2008; 36(7): 391-396.
17. Lee W., Kalache K.D., Chaiworapongsa T., Londono J., Treadwell M.C., Johnson A., Romero R., Three-dimensional power Doppler ultrasonography during pregnancy. J. Ultrasound Med. 2003; 22(1): 91-7.
18. Hafner E., Metzenbauer M., Hofinger D., et al. Placental growth from the first to the second trimester of pregnancy in SGA-foetuses and pre-eclamptic pregnancies compared to normal foetuses. Placenta 2003; 24: 336.
19. Carmen Mihaela Mihu, D Mihu, N. Costin, S. Dudea, Mihaela Oancea, R. Ciortea. Aportul ecografiei 3D power Doppler în evaluarea circulației feto-placentare. Gineco.ro 2009; 4: 224-228.
20. Matijevic R., Kurjak A., The assessment of placental blood vessels by three-dimensional power Doppler ultrasound. J. Perinat. Med. 2002; 30(1): 26-32.