ORIGINAL ARTICLE

Ultrasound and Doppler Assessment of Fetuses with Growth Restriction in the Absence of an Evident Etiological Factor

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Background: Differentiation between normal and pathological fetal growth may be difficult and a regular fetal biometry is required, with ultrasound examination of the placenta, amniotic fluid index assessment and Doppler velocimetry of pregnancies with fetal growth disorders, even in the absence of a clear etiologic factor.
Material and method: This is an observational study and includes two groups: one with 24 pregnancies with FGR confirmed postpartum (SGA+) and another with 42 pregnancies with normal birth weight (SGA-). The database contained personal data, several parameters of fetal biometry, amniotic fluid index, placentation and velocimetric indices, birth-related data. Statistical analysis of obtained data was carried out using Microsoft Excel and Graphpad Prisma programs. We used the Student test, Z test and Chi square test and Fisher when needed. P <0.05 was considered statistically significant. We also used Pearson correlation index.
Results: Between the two groups there were statistically significant differences regarding fetal biometry parameters, especially AC and ultrasound estimated weight and birth weight, infant length, Apgar score at 5' and days of hospitalization. Velocimetric indices were significantly higher in placental uterine and umbilical artery in SGA+ group. There was a negative correlation between umbilical RI and AFI in SGA+ group but without statistical significance.
Conclusions: Fetal biometry, umbilical artery Doppler examination (when RI <0.6) and AFI calculation (>10) are the most used methods in the assessment of normal fetal growth and intrauterine fetal wellbeing.

Keywords: IUGR, eco Doppler, placental insufficiency

Introduction

The term small for gestational age (SGA) was initially used for newborn babies but it is also used for fetuses, often being replaced by the term intrauterine growth restriction (IUGR) or fetal growth restriction (FGR). The latter (FGR) is defined after estimated fetal weight (EFW), that is ≤10th percentile for gestational age [1,2,3], a definition of Battaglia and Lubchenco initially described in 1967, followed by other definitions including ≤ 3rd or 5th percentile or below 2 SD from the mean.

The lack of sensitivity and specificity of growth curves drawn so far prevent from establishing the exact diagnosis of IUGR (inappropriate for many fetuses). Therefore growth curves are necessary to include more variables that influence fetal size [4], many of small children at birth being SGA only because of maternal constitutional factors (≈ 70% of fetuses with estimated weight below the 10th percentile) [3,5].

The purpose of this paper is to highlight the importance of finding fetal growth disorders even without a clear etiological factor by a regular fetal biometry, ultrasound examination of the placenta, amniotic fluid index assessment and Doppler velocimetry and for differentiating SGA fetuses without hemodynamic changes from those with IUGR and also with circulatory adaptive signs to hypoxia [6,7].

Material and method

The study is an observational study and includes a number of 66 pregnant women examined in the third quarter of pregnancy and admitted to the Obstetrics and Gynecology Clinic II of the Mureș County Emergency Clinical Hospital (02/15/2008 to 03/15/2011), on which in the absence of any risk factor for IUGR (excluding also maternal or fetal-annexial causes) a difference of 2 to 5 weeks between the chronological age and ultrasound age in the third quarter of pregnancy was observed.

Pregnant women examined were divided into two groups: one which included 24 pregnancies with FGR confirmed postpartum (SGA+) and the second consis-ting of 42 pregnancies where the babies at birth had a normal weight (AGA – adequate for gestational age).

The study aimed to analyze the changes in placental circulation by integrating the Doppler ultrasound as a traditional method of exploring fetal assessment.

Ultrasound examinations were performed by a single examiner (the author), with the device LOGIQ S6 produced by General Electric HealthCare in 2006 and data collection was based on a research form.

The database included:

- Personal details – age of pregnant women, the environment of origin, socio-economic conditions, education, body mass index;
- Fetal biometry – biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), femur length (FL), ratios: FL/HC, FL/AC, HC/AC, estimated fetal weight (EFW);
- Placentation – location, thickness, degree of maturation (after Granuum);

Table I. Descriptive study of the mean ages and body mass index in the 2 groups

	SGA+		SGA–		p value
	Mean	SD	Mean	SD	
Age	24.21	5.35	25.62	6.99	0.3962
Body Mass Index	26.31	5.16	27.32	3.50	0.3464

- Amniotic fluid index (AFI);
- Doppler velocimetry – resistance index (RI), pulsed index (PI), systolic-diastolic index (S/D) placental uterine arteries (PUA), non-placental uterine arteries (NPUA), umbilical artery (UA), middle cerebral artery (MCA), cerebro-placental ratio (CPR);
- Non-stress test (NST);
- Data regarding birth: gestational age, mode of delivery (spontaneous, oxitocin perfusion or by caesarean section), Apgar score, weight, length, duration of hospitalization, weight at discharge.

The statistical analysis of the obtained data was done in Microsoft Excel and Graphpad Prisma. We followed parameters in the descriptive statistics (mean, standard deviation) for the description of characteristics of the groups and we compared the same type of values between the two groups using Student test, the Z test for calculating difference between two proportions, and based on contingency table 2 × 2 Chi square test and Ficher test was applied. A p value of less than 0.05 was considered statistically significant. We also used Pearson correlation index and tables and graphs for nominal and ordinal data.

Results

Applying the Student test we found that there was no statistically significant difference between the mean ages of the two groups (p = 0.3962), or their body mass index (p = 0.3464) (Table I).

Table II. The difference between the two groups education, socio-economic conditions and delivery way in the 2 groups

		SGA+		SGA–		p value
		Mean	SD	Mean	SD	
Studies	Without	4	16.7	3	7.1	0.70
	Primary	6	25	8	19	0.78
	Secondary	11	45.8	21	50	0.98
	Advanced	3	12.5	10	23.8	0.97
Socio-economic conditions*	Very Good	2	8.3	3	7.1	0.96
	Good	8	33.3	22	52.4	0.87
	Media	3	12.5	10	23.8	0.88
	Weak	11	45.8	5	11.9	0.18
	Very Weak	0	0	2	4.8	–
Delivery way	Caesarean	6	25	9	24.4	0.87
	Oxytocin perfusion	6	25	17	40.5	0.93
	Oxytocin perfusion and "Bracht"	2	8.33	0	0	–
	Spontaneous	10	41.6	16	38.1	0.85

*According to National Institute of Statistics: media conditions-having the median salary per economy; weak-below the median salary per economy; very weak-without salary; good-twice median salary per economy; very good-more than twice median salary per economy.

Applying Fisher's test we also found that there was no statistically significant difference between rural and urban environments of the two groups (p = 0.2080).

Applying the Z test between the two groups we found a p >0.05 for patients education, socio-economic conditions, with no statistically significant difference also between the types of birth for pregnancies in the 2 groups (Table II).

Descriptive study of gestational age, fetal biometry, the thickness of the placenta, amniotic fluid and dates of birth or after the birth are given in Table III.

The difference between the sexes at birth was not statistically significant as reflected by the Fisher test applied: p = 0.4394.

Distribution of fetuses from both groups based on weight and gestational age can be seen in Figures 1 and 2.

Fig. 1. Distribution of fetuses according to estimated weight and ultrasound gestational age in group SGA+

Fig. 2. Distribution of fetuses according to estimated weight and ultrasound gestational age in group SGA–

Table III. Descriptive study of gestational age, fetal biometry, thickness of the placenta, amniotic fluid index, dates of birth and after birth respectively in the 2 groups

		SGA+		SGA–		p value
		Mean	SD	Mean	SD	
Gestational age (days)	Chronological	267.17	15.85	273.40	14.01	0.1022
	Ultrasound	243.88	11.32	254.05	9.99	0.0003
Fetal biometry	DBP	8.75	0.48	9.10	0.41	0.0036
	HC	31.04	1.44	32.30	1.14	0.0003
	AC	29.22	1.88	31.92	2.10	0.0001
	LF (cm)	6.91	0.52	7.22	0.35	0.0066
	EFW (g)	2374.75	366.17	2862.10	391.14	0.0001
	LF/HC	0.22	0.01	0.22	0,012	0.9961
	LF/AC	0.235	0.02	0.223	0.01	0.0087
	HC/AC	1.06	0.06	1.01	0.06	0.0027
Placenta	Thickness (cm)	3.46	0.51	3.54	0.57	0.5975
AFI	Index (AFI) (cm)	12.63	4,31	12.04	4,27	0.5898
Birth related data	Apgar score (1')	8.5	1,1	9	0.58	0.26
	Apgar score (5')	9	0,79	9,5	0,5	0.02
	Weight (g)	2542.08	305.85	3323.57	343.47	0.0001
	Length (cm)	47.58	1.97	50.21	1.93	0.0001
After birth	Hospital days	7.45	4,17	5.71	1,4	0.05
	Weight (g)	2598,3	164.70	3240.7	326.72	0.0001

Table IV. Descriptive study of the velocimetric indices in the 2 groups

Artery	Velocimetric indices	SGA+		SGA–		p value
		Mean	SD	Mean	SD	
Uterine (PUA)	RI	0.48	0.11	0.42	0.08	0.0209
	PI	0.75	0.24	0.61	0.16	0.0064
	S/D	2.03	0.48	1.77	0.27	0.0096
Uterine (NPUA)	RI	0.52	0.07	0.48	0.11	0.1600
	PI	0.83	0.20	0.75	0.32	0.2782
	S/D	2.14	0.36	2.05	0.67	0.5641
Umbilical (UA)	RI	0.60	0.06	0.53	0.08	0.0010
	PI	0.93	0.14	0.77	0.17	0.0005
	S/D	2.58	0.43	2.21	0.40	0.0009
Middle Cerebral (MCA)	RI	0.71	0.07	0.70	0.09	0.5526
	PI	1.32	0.28	1.30	0.38	0.7903
	S/D	3.84	1.20	3.56	1.21	0.3748
Ratio	RCP (Arbeille I.)	1.20	0.15	1.33	0.20	0.0058
	UMB PI/CER PI	0.72	0.03	0.62	0.02	0.0147

Mean and standard deviation of velocimetric indices are presented in Table IV.

There was no statistically significant difference between levels of maturity of the placenta between the two groups nor between the placental vascularization in the 2 groups as shown in Table V.

Also, there was no significant correlation between the RI of UA and AFI, estimated fetal weight and birth weight between the two groups (Table VI).

Discussions

As it can be seen in the results presented (Table I and II), unlike other more complex studies [4,5] between the two groups there was no statistically significant difference (p >0.05) regarding patients' age, environment provenance, studies, socio-economic status, body mass index, although in the SGA+ group the proportion of patients without education was 2 times higher compared with the SGA– group and the percentage of patients with weak socio-economic conditions in group SGA+ is approximately four times higher compared with the SGA– group.

Chronological age of pregnancies was not significantly different in the two groups, but after performing fetal biometry there was a statistically significant difference between the most important parameters measured: BPD, HC, AC, FL, and obviously between estimated fetal weight (EFW) by Hadlock [6]. These parameters are the most often used to evaluate intrauterine fetal growth and changes of some ratios (FL/AC, HC/AC) [6,7], and as it was evident from our study, can also appreciate asymmetric fetal growth restriction (FL/AC >0.24) (Table III) [1].

Distribution of fetuses by weight and gestational age (Figures 1 and 2) show a clear difference between the two groups and the weight at birth and at discharge was significantly lower in the SGA+ group compared with the SGA– group (p = 0.0001). Prolonged hospitalization was found especially in cases where prematurity was involved.

Oligohydramnios (in our study when AFI <10) may be an early marker of the decline of placental function [1,2,8] and sometimes could be present before finding obvious ecoDoppler changes in the umbilical artery. The difference was not statistically significant between the 2 groups concerning AFI, although raised velocimetric indices were

Table V. The difference between the two groups on placental degree and vascularization

		SGA+		SGA–		p value
		NR (24)	%	NR (42)	%	
Placental degree (after Granuum)	2	7	29.2	6	14.3	0.51
	2/3	7	29.2	17	40.5	0.95
	3	10	41.6	19	45.2	0.82
Placental vascularization**	Well represented	2	8.33	8	19	0.94
	Normal	1	4.16	14	33.3	0.87
	Relatively normal	17	70.8	20	47.7	0.15
	Reduced in middle1/3	4	16.66	0	0	–

**well represented: with multiple visible vascular branches between chorial and basal plate; normal: 4-5 vascular branches; relatively normal: 3-4 vascular branches; reduced in middle 1/3: only 1-2 vessels are visible under chorial plate.

Table VI. Correlations between different indices and RI of the umbilical artery in the 2 groups

Pearson correlation	SGA+ UA RI		SGA– UA RI	
PUA RI	r = -0.14	p = 0.49	r = 0.11	p = 0.47
AFI	r = -0.30	p = 0.15	r = 0.32	p = 0.03
EFW	r = -0.06	p = 0.76	r = -0.28	p = 0.06
Birth weight	r = 0.07	p = 0.73	r = -0.20	p = 0.19

found in the umbilical artery of fetuses in the SGA+ group, the difference in these indices being statistically significant (Table IV).

The increase of umbilical artery Doppler indices, a recording of an absent, or worse, a reversed diastolic flow in the umbilical artery would allow assessment of the degree of placental insufficiency and the status of a fetus with IUGR [2,9]. Changes of velocimetric indices in uterine and umbilical artery in our study were minor (mild placental dysfunction) and no changes were found in the middle cerebral artery, the difference being insignificant. CPR ratio although >1 and only sporadically = 1 (in a single case <1) was significantly lower in the SGA+ group, as well as UMB PI/CER PI ratio, and Apgar score at 5' was lower in SGA+ fetuses. These minor changes of fetal hemodynamics include the fetuses from this study in stage I of fetal adaptation in the context of their changing growth potential [10].

The thickness of the placenta, the degree of maturation and the vascularization in the placenta (assessed with color/power Doppler by the number of branching subchorial vessels) did not differ significantly in the two groups, although the FGR in the SGA+ group was considered idiopathic due to a mild placental dysfunction occurred in the second part of the pregnancies.

Because the perinatal mortality in children with IUGR is 6–10 times higher than in children with normal growth [7], an early diagnosis of IUGR is required, based mainly on echographic examination.

In our study there were no babies born with severe restriction or postnatal adaptation difficulties and there was no death recorded, except for one case in which the fetus died in utero at about 10 days after the ultrasound found a FGR (<5%) and a CPR ratio <1.

Non-stress test (NST) performed by routine was responsive to all patients as we expected, because cardiotocographical changes are observed at a variable period of time after velocimetric changes [10]. It is therefore not necessary to perform NST in pregnant women with a RI in umbilical artery that is below 0.6 and especially below 0.55.

Even if there is not an internationally accepted clinical definition for IUGR, the birth weight and gestational age still remain important for the evolution of new-born babies [11,12,13,14].

There is no need for an intensive antenatal surveillance of fetuses with normal umbilical artery flow (especially normal S/D ratio) and normal amniotic fluid index (AFI) [1,7] as evident from our study.

Conclusions

Classic ultrasound remains the primary method of diagnosis of IUGR and Doppler examination allows assessment of the functional reserves of a fetus showing a slowdown or stagnation of intrauterine growth.

Umbilical artery is the most common site used in the assessment of intrauterine fetal condition and an RI ≥0.6 in the third trimester of pregnancy requires careful monitoring of pregnancies, especially if there was a growth disorder, even in the absence of clinically apparent causes.

The decision concerning the moment of birth depends on dynamic Doppler changes, but also on gestational age and fetal weight estimated by fetal biometry.

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