The analysis of doppler flow alterations in intrauterine growth restricted pregnancies

Burcu Artunc Ulkumen[1], H. Gursoy Pala[1], Fatma Eskicioglu[1], Yesim Baytur[1]

Abstract

Objective: Intrauterine growth restriction (IUGR) is a common clinical condition. For some clinicians, it is still not clear which patients should be referred to a tertiary center. In this study, we aimed to analyse the sonographic parameters of IUGR suspected pregnancies and find out which finding is the most sensitive in the diagnosis of IUGR.

Methods: Doppler flow findings and biometric measurements of 50 IUGR suspected pregnancies admitted to our perinatology outpatient clinic between March 2013 and March 2014 were evaluated. 60 healthy singleton pregnancies were assigned as the control group. The same measurement were performed and compared. The diagnosis of IUGR was made on one of the followings: AC measurement < 10 p, uterine artery RI >0.58, the fetal growth rate < 10 p, fetal weight < 10 p. Gestational week was calculated regarding the last menstrual period and confirmed with the first trimester ultrasonographic findings.

Results: In IUGR and control group, maternal age was 26.63 ± 5.19 and 29.48 ± 5.79, respectively (p=0.327); gravida was 1.74 ± 0.99 and 2.13 ± 1.51 (p=0.290); parity was 0.63 ± 0.89 and 0.98 ± 0.49, (p=0.703); gestational week was 34.82 ± 3.27 and 34.21 ± 4.07 (p=0.70), respectively. Umbilical artery PI was 1.51 ± 0.96 in IUGR group and 1.00 ± 0.22 in control group (p<0.001). Fetal MCA PI was significantly lower in IUGR group (1.61 ± 1.57 vs 1.98 ± 0.74; p=0.005). AUC values obtained by ROC analysis were as following: 0.590 for HC/AC; 0.655 for UA/MCA ratio; 0.622 for Oligohydramnios; 0.559 for UA PI.

Conclusions: HC/AC ratio >1 and umbilical artery PI >0.95 have the highest sensitivity for IUGR (Sensitivity 82% and 80%; specificity 56% and 44%, respectively). Oligohydramnios and UA/MCA PI ratio were shown to have the highest specificity (specificity 70%).

Keywords: IUGR, HC/AC, Oligohydramnios, umbilical artery PI, cerebral artery PI.

Introduction

Intrauterine growth restriction (IUGR) is the clinical condition which is characterized by the decrease in fetal growth and failure of the fetus to reach its growth potential (1). The incidence of IUGR is approximately 5-7% (2).

Fetal growth occurs in 3 phases: fetal cell hyperplasia in early pregnancy; fetal cell hyperplasia and hypertrophy followed by fetal cell hypertrophy in the third trimester. Fetal growth is 5 g/day for the first trimester, 10 g/day for the mid-trimester and 30-35 g/day in the third trimester (especially after 32-34 gestational weeks) (3).

The lack of appropriate fetal growth is classified in two main groups: asymmetric IUGR with decreased subcutaneous fat tissue and symmetric IUGR with decreased growth in all body parts of the fetus. Chromosomal abnormalities, structural anomalies, intrauterine infection and toxic agents may be the cause of symmetric IUGR by affecting the fetal growth. However, most cases with IUGR occur due to uteroplacental insufficiency with significant risk for fetal hypoxia (1).

The clinicians were used to evaluate the fetal growth according the population-based growth charts and fetal measurements below 10 percentile (p) were regarded as a pathological condition. However, the current trend is to construct the individual growth charts for every fetus, because poor perinatal outcomes are rare in fetuses below 10 p who has reached its genetic growth potential (called as "small gestational age-SGA"); in the other hand, a fetus between 10-20 p without reaching its growth potential (called IUGR) is prone for adverse perinatal outcomes (2). The differential diagnosis between SGA and IUGR fetuses is important to predict perinatal outcomes. Determination of fetal growth rate and fetal functions evaluated with amniotic fluid index (AFI) and umbilical artery Doppler is corner stone in differentiation of both conditions (3,4).

Material and Methods

Doppler flow and biometric measurements of 50 IUGR suspected pregnancies who admitted to perinatology outpatient clinic between March 2013 and March 2014 are analyzed in this study. 60 healthy singleton pregnancies are randomly selected as control group.

The diagnosis of IUGR is based on the lack of the fetal growth on subsequent measurements repeated in 2 weeks. Gestational week is calculated according to the last menstrual date and early first trimester sonographic findings. The measurements are performed with Voluson 730 (GE Medical Systems, Milwaukee, WI) 3,5-MHz abdominal probe. All measurements are performed by two operators (BAU and HGP).

Bi-parietal diameter (BPD) is measured "in to out" at the level of inter-hemispheric fissure and thalamic nuclei. Head circumference (HC) is measured at the same level. Abdominal circumference (AC) is measured when liver, the horizontal part of portal vein, stomach and fetal vertebra are seen at the same circumferential level.

AFI is calculated with the sum of the four vertical pocket measurements. Oligohydramnios is AFI <5 cm. Umbilical artery Doppler evaluation is performed in free loop. Fetal middle cerebral artery Doppler evaluation (MCA) is performed at the proximal one third of Willis polygon. Three consecutive wave forms are needed for the calculations.

Statistical analysis is made with SPSS v.20. T-test is used for the comparison of the groups. The results are expressed in mean±standard deviation (SD). The significance of the markers for the IUGR diagnosis is defined with ROC analysis. AUC (area under the curve) is calculated. The sensitivity and specificity is determined according the ROC analysis.

Results

The mean maternal age was 26.63 ± 5.19 in IUGR and 29.48 ± 5.79 in control group, respectively (p=0.327). The mean gravida was 1.74 ± 0.99 and 2.13 ± 1.51 (p=0.29), the mean parity was 0.63 ± 0.89 and 0.98 ± 0.49 (p=0.703), the mean gestational week was 34.82 ± 3.27 and 34.21 ± 4.07 (p=0.70) in IUGR and control groups, respectively. Umbilical artery (UA) pulsatility index (PI) was 1.51 ± 0.96 in IUGR and 1.00 ± 0.22 in control group (p<0.001).

Fetal middle cerebral artery (MCA) PI was 1.61 ± 1.57 in IUGR group and 1.98 ± 0.74 in control group (p=0.005). UA PI was significantly higher and MCA PI is significantly lower in IUGR group (Table 1-2). In ROC analysis, AUC of ultrasonographic results for IUGR diagnosis was as following: HC/AC 0.590; Umbilical/cerebral PI

0.655, Oligohydramnios 0.622, UA PI 0.559. HC/AC ratio (>1) and UA PI (>0.95) had the highest sensitivity (sensitivity 82% and 80%; respectively.

Specificity 56% and 44%, respectively). Oligohydramnios and umbilical/cerebral PI ratio was the most specific findings with 70% specificity (Figure 1-2; Table-3).

Table 1: The comparison of demographic features of IUGR and control groups (Mean±**SD**)

	IUGR (n:50)	Control (n:60)	p
Maternal age	26.63±5.19	29.48±5.79	0.327
Gravida	1.74±0.99	2.13±1.51	0.290
Parity	0.63±0.89	0.98±0.49	0.703
Gest. week	34.82±3.27	34.21±4.07	0.700

Table 2: The comparison of clinical features of IUGR and control groups (Mean±**SD**)

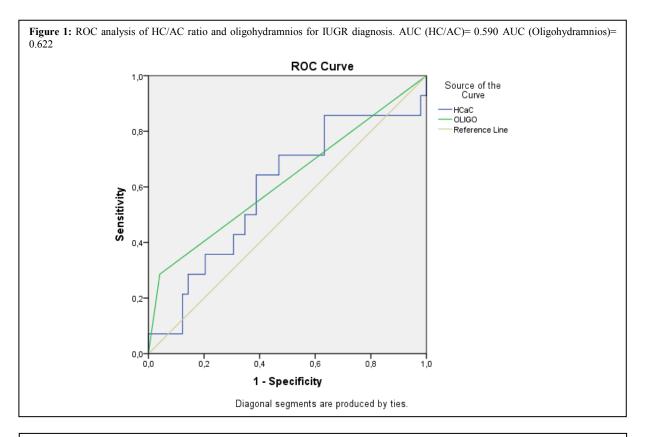|	IUGR (n:50)	Control (n:60)	p
U.A. PI	1.51±0.96	1.00±0.22	0.001
MCA PI	1.61±1.57	1.98±0.74	0.005
AFI	7.44±4.78	14.23±5.02	0.001
EFW	2080.21±692.35	2405.33±972.70	0.005

U.A. PI: Umbilical Artery MCA: mid-cerebral artery; PI: pulsatility index; AFI: amniotic fluid indekx; EFW: estimated fetal weight
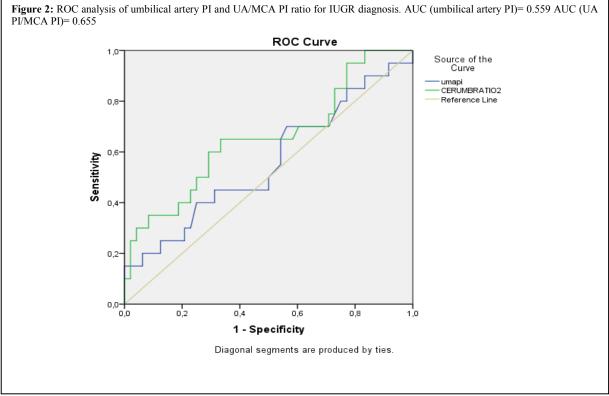
Table 3: The sensitivity and specificity of ultrasonographic findings

	Cut-off value	Sensitivity	Specificity
HC/AC	1.02	% 82	% 56
Oligohydramnios	≤5 cm	% 45	% 70
U.A. PI	0.95	% 80	% 45
UA/MCA PI	0.63	% 65	% 70

Discussion

In this study, we aimed to define the sensitivity of the sonographic findings in the diagnosis and management of IUGR suspected pregnancies. The first task in evaluating IUGR suspected pregnancy is to specify the gestational week accurately. The first trimester ultrasonographic scans with CRL measurements are most helpful with specifying the gestational week ±3 days (7).

The sonographic scans between 16-21 weeks may be mistaken for 10 days. The second task should be subsequent measurements of fetal growth with documentation of the lack of the fetal growth. Regarding IUGR cases with ongoing utero-placental insufficiency, accurate timing of the delivery is very important due to fetal hypoxia and

Figure 1: ROC analysis of HC/AC ratio and oligohydramnios for IUGR diagnosis. AUC (HC/AC)= 0.590 AUC (Oligohydramnios)= 0.622

Figure 2: ROC analysis of umbilical artery PI and UA/MCA PI ratio for IUGR diagnosis. AUC (umbilical artery PI)= 0.559 AUC (UA PI/MCA PI)= 0.655

adverse perinatal outcome risks. The timing of delivery should be defined according to the gestational week, fetal presentation, and fetal Doppler flow findings (8).

Doppler evaluation is one of the most useful tools for fetal wellfare. UA Doppler study evaluates the resistance against the perfusion in feto-placental unit. Most commonly used clinical markers are pulsatility index (PI) and systolic/diastolic flow ratio (S/D).

PI is more useful, as S/D ratio could not be measured when absent end-diastolic flow occurs in

umbilical artery (9). Normal UA flow pattern is characterized by the low resistance and high end-diastolic flow (10). UA Doppler measurement may be performed in any segment; however, of clinical importance in interpreting the results: near the placental end, the end-diastolic flow increases; near the abdominal insertion of the cord, the resistance increases and end-diastolic flow decreases (11).

We performed all measurements at the free loop and we obtained at least three consecutive wave forms. UA PI was significantly higher in IUGR group (p<0.001). If cut-off value for UA PI was regarded as 0.95, sensitivity was 80% and specificity was 45%. In an another study, UA PI sensitivity was found 46.7% (12). Our results are in agreement that UA PI is clinical useful to differentiate IUGR and SGA fetus.

Cerebral circulation has high resistance and characterized with continuous forward flow

during a complete heart cycle (13). MCA provides 80% of the cerebral circulation. Besides, the measurements are obtained most easily among other fetal cerebral vasculature (14). That is why MCA is used for evaluation of IUGR fetuses. The measurement is performed ideally at the one third proximal segments near to Willis polygon (15). In case of fetal hypoxia, due to central redistribution, blood supply increases to adrenal gland and heart, whereas blood supply decreases to peripheric pathways.

This condition is defined as "brain sparing effect" and characterized with low PI (so, increased end-diastolic flow) (16). Brain sparing effect (BSE) can be also evaluated with cerebra-placental ratio (MCA/UA PI). BSE occurs if this ratio is below 5p according to the gestational week (17, 18). Gramellini et al. showed that MCA/UA PI remained stable during the last 10 gestational weeks (19). MCA PI was significantly lower in our IUGR group (p=0.005). However, MCA PI alone was not useful. If cut-off value for UA/MCA PI was regarded as 0.63, sensitivity was 65% and specificity was 70%.

The main limitations of our study were the retrospective design and the lack of the perinatal outcomes. Doppler studies are controversial in evaluating the low-risk pregnancies. The current trend suggests that routine Doppler evaluation does not add anything, so routine screening is not recommended (9, 20). Regarding the IUGR cases, the frequency of UA Doppler measurements is also controversial, because there are not enough randomized controlled studies (21). UA Doppler measurements can be repeated in every 2 weeks with non-stress test (NST) and AFI 2 times a week in IUGR with utero-placental insufficiency (21-23). If any abnormality is detected in Doppler studies, it can be repeated every week, unless end-diastolic

flow gets lost (8). However, if there is Oligohydramnios or if there is absent end-diastolic flow in UA, then Doppler evaluation should be repeated 2-3 times in a week (25). If the pregnancy is below 34 weeks with absent end-diastolic flow in UA, daily ductus venosus (DV) Doppler and biophysical profile analysis is recommended.

Absent or reverse a-wave in DV Doppler, biophysical profile <6 or spontaneous persistent decelerations in NST are the findings for delivery. If the pregnancy is below 34 weeks with reverse flow in UA, the fetus should be delivered. If the pregnancy is beyond 34 weeks with absent end-diastolic flow, the fetus should be again delivered.

As a result, umbilical artery Doppler studies are the most important tool for defining the IUGR pregnancies. UA Doppler is easy to perform. Clinicians in peripheric health care centers may use of UA Doppler in deciding to refer the high risk pregnancies to a tertiary perinatology unit.

Conflict of Interest: The authors declared that they had no conflicts of interest.

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