Published online: 02/02/2016 Published print:02/2016

ORIGINAL PAPER

Hepato - Cephalic Index as a Predictor of Intrauterine Growth Restriction

Ramadan Dacaj[1], Sebija Izetbegovic[2], Goran Stojkanovic[2], Curr Gjocaj[3]

[1]Department of Obstetrics and Gynecology, Regional Hospital, Pec, Republic of Kosova
[2]Department of Gynecology and Obstetrics, General Hospital „Prim. Dr. Abdulah Nakas", Bosnia and Herzegovina
[3]University Hospital Clinical Services, Prishtina, Republic of Kosova

Corresponding author: Ramadan Dacaj, PhD. Department of Obstetrics and Gynecology, Regional Hospital, Pec, Republic of Kosova. ORCID ID: http://orcid.org/0000-0002-0178-7066 E-mail: ramadandacaj@gmail.com

doi: 10.5455/aim.2016.24.12-15

ACTA INFORM MED. 2016 FEB; 24(1): 12-15

Received: 11 November 2015 • Accepted: 15 January 2016

© 2016 Ramadan Dacaj, Sebija Izetbegovic, Goran Stojkanovic, Curr Gjocaj

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Aim: The aims of this study were to compare ultrasound fetoplacental parameters and to calculate Hepato-Cephalic Index (HCI) as a new predictor of IUGR. **Methods and material:** A clinical prospective study was conducted and included 120 pregnant women divided in two groups: non IUGR group included healthy pregnant women *(n=60)* and IUGR group included pregnant women with preeclampsia and IUGR (n=60). Outcome measures were following ultrasound fetoplacental parameters in fetuses with IUGR and non IUGR: Fetal Liver Length (FLL), Femur Length (FL), Biparietal Diameter (BPD), Placental Maturation by Grannum, Amniotic Fluid Index (AFI) and Hepato-Cephalic Index (HCI). Sonography was carried out by probe 3.5 Mhz type MINDRAY DC 7. **Results:** The mean of maternal age was 30.0±6.1 years in women with preeclampsia and IUGR and 28.1±5.1 years in healthy pregnant women, $p > 0.05$. There was a statistically significant difference in values of: FLL ($p < 0.001$), FL ($p = 0.004$), BPD ($p < 0.001$), AFI ($p < 0.001$), HCI ($p < 0.001$) between IUGR and non IUGR groups. The most of women with preeclampsia and IUGR had grade III of placental maturation (48.3%). There is a significant association between the placental maturation and the diagnosis, $p < 0.001$. There was a statistically significant difference in body mass of newborns between IUGR and non IUGR groups, $p < 0.001$. **Conclusion:** In a fetus with IUGR in preeclampsia there is a reduction in FLL, FL, BPD, AFI and HCI and there is a early maturation of the placenta. By measurement of fetoplacental ultrasonic parameters of liver, pregnant women will experience prediction of risk pregnancy (preeclampsia with IUGR) due to hypoxia.

Key words: Preeclampsia, intrauterine growth restriction, ultrasound fetoplacental parameters, hepato-cephalic index.

1. INTRODUCTION

Intrauterine Growth Restriction (IUGR) is the term used to describe a fetus that has not reached its growth potential because of fetal, placental, or maternal factors. It is defined as an estimated fetal weight <10^{th} percentile. Clinically, most infants with IUGR are identified because they are born small for gestational age (SGA) which is defined as a weight less than a specified percentile (usually the 10th percentile) (1). Clinical assessment alone is not adequate in pregnancies at high risk for IUGR, given the low sensitivity and specificity. There is a general consensus that once the suspicion of FGR has arisen because of risk factors or physical examination, sonographic techniques should be used to try to confirm or exclude the diagnosis (2, 3, 4). Identification of IUGR infants is important because these infants are at increased risk of perinatal morbidity and mortality and affects approximately 7–15% of worldwide pregnancies (1, 5). A variety of sonographic parameters have been used to diagnose IUGR. Most studies report reduced abdominal circumference (AC) is the most sensitive single morphometric indicator of FGR (6, 7, 8, 9). Although the size of the fetal liver may be reduced as a result of fetal malnutrition, this is a less sensitive marker for IUGR than AC (10, 11). Measurement of AC was more predictive of FGR than measurement of either head circumference (HC) or biparietal diameter (BPD) or the combination of AC with either one of these two variables. In 1975, Campbell and Wilkin first published a regression equation for estimating fetal weight based upon sonographic measurement of the AC and HC (12). Other equations have been published subsequently using two or more morphometric body measurements (e.g., BPD, AC, HC, occipital frontal diameter, abdominal diameter, transthoracic circumference, and femur length (FL)) to improve sonographic accuracy (13, 14, 15, 16).

The aims of this study were to compare ultrasound fetoplacental parameters and to calculate Hepato - Cephalic Index as a new predictor of IUGR.

2. MATERIALS AND METHODS

A clinical prospective study was conducted and included 120 pregnant women divided in two groups: non IUGR group included healthy pregnant women (n=60) and IUGR group included pregnant women with preeclampsia and IUGR (n=60). Preeclampsia was determined with method of Last Menstrual Period (LMP), Hadlock's formula on the basis of presence of proteinuria (> 0.5 g/L) and high blood pressure (TA = 140/90 mmHg) (17). Antenatal diagnosis of IUGR was based on sonographic evaluation of the fetus, placenta, and amniotic fluid. Sonography was carried out by probe 3.5 Mhz type MINDRAY DC 7.

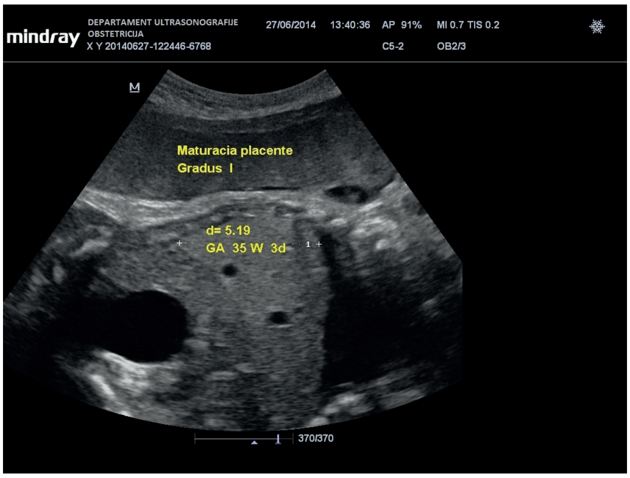

Figure 1. Measurement of FLL (d = length of right lobe of liver, 5.19 cm; GA = Gestational age, 35 weeks and 3 days)

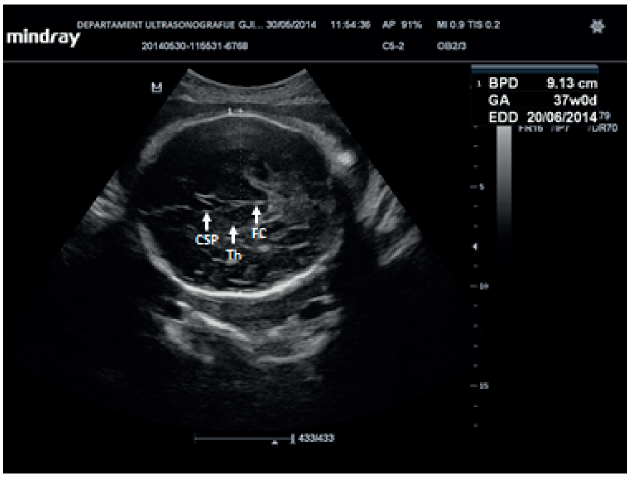

Figure 2. Measurement of BPD (CSP = Cavum septi pellucidi; Th = Thalamus; FC = Falx cerebri)

Outcome measures were following ultrasound fetoplacental parameters in fetuses with IUGR and non IUGR: Fetal Liver Length (FLL), Femur Length (FL), Biparietal Diameter (BPD), placental maturation by Grannum and Amniotic Fluid Index (AFI), Hepato-Cephalic Index (HCI) (Figure 1 and 2).

Results are expressed as mean value and standard deviation in case of normal distributed continue variables, as median and interquartile range (IQR) in case of non-normal distributed continue variables. The inspection of histograms and quantile diagrams and the Kolmogorov–Smirnov test with a Lilliefors significance level were used for testing normality of distribution of continuous numerical variables. In case of categorical variables, counts and percentages were reported. Categorical data were analyzed with Pearson's Chi-Square test or Fisher's Exact test. Statistical analysis comparing the two groups was performed with Independent Sample T-test for continuous normal distributed variables and Mann–Whitney U-test for continuous non-normal distributed variables. A p-value <0.05 was considered as significant. Statistical analysis was performed by using the Statistical Package for the Social Sciences (SPSS Release 19.0; SPSS Inc., Chicago, Illinois,United States of America) software.

3. RESULTS

The mean of maternal age was 30.0±6.1 years in women with preeclampsia and IUGR and 28.1±5.1 years in healthy pregnant women. There is no statistically significant difference in maternal age distribution between two groups (p> 0.05). The most of women with preeclampsia and IUGR had grade III of placental maturation (48.3%) (Figure 3). There is a significant association between the placental maturation and the diagnosis ($Hi^2(3) = 24.216$; $p < 0.001$).

Note: Continuous variables are expressed as median with interquartile range (IQR, 25th to 75th percentiles), statistics by Mann-Whitney. Fetuses in IUZR group had lower median value of FLL (Me = 42.0 mm, IQR = 40.9 to 42.7) compared to non IUZR group (Me = 54.6 mm, IQR = 44.1 to 56.4). There is a statistically significant difference in median value of FLL between these two groups, U = 754.000, z = -5.501, p < 0.001. Fetuses in IUZR group had lower median value of FL (Me = 65.5 mm, IQR = 61.5 to 69.5) compared to

Variables	IUGR	non IUGR	p-value
	(n=60)	(n=60)	
Age (yrs)	30.0±6.1	28.1±5.1	0.079
Week of gestation	37 (32 to 38)	38 (36 to 39)	0.068
Stage of placental maturation (%)			
0	3.3	13.3	<0.001
I	16.7	38.3	
II	31.7	38.3	
III	48.3	10.1	

Table 1. Characteristics of pregnant woman in both groups

Variables	IUGR	non IUGR	p-value
	(n=60)	(n=60)	
FLL (mm)	42.0 (40.9 to 42.7)	54.6 (44.1 to 56.4)	<0.001
FL (mm)	65.5 (61.5 to 69.5)	71.6 (60.5 to 72.8)	0.004
BPD (mm)	84.6 (80.0 to 86.4)	92.4 (82.3 to 93.5)	<0.001
AFI (cm)	6.5 (4.5 to 11.0)	14.3 (12.3 to 15.7)	<0.001

Table 2. Ultrasound fetoplacental parameters in fetuses with IUGR and non IUGR. Note: Continuous variables are expressed as median with interquartile range (IQR, 25th to 75th percentiles), statistics by Mann-Whitney. Definition of abbreviations, IUGR = Intrauterine growth restriction; FLL = Fetal Liver Length; FL = Femur Length; BPD = Biparietal diameter; AFI = Amniotic Fluid Index.

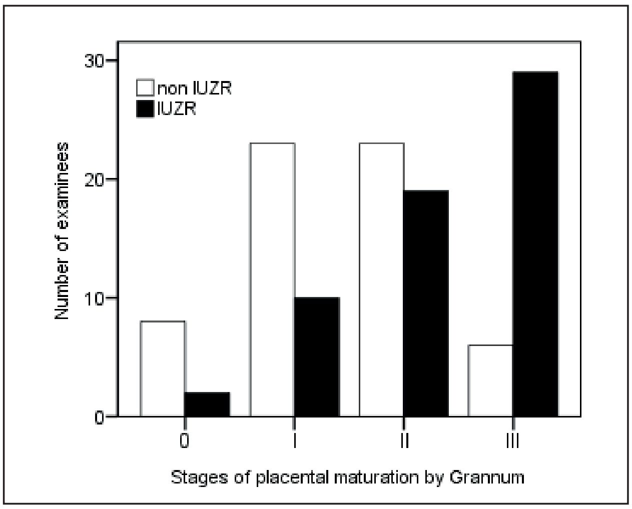

Figure 3. Stages of placental maturation by Grannum in non IUGR and IUGR groups

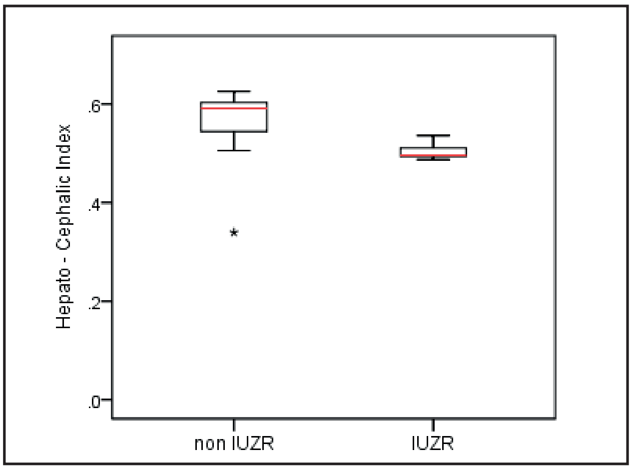

Figure 4. Hepato–Cephalic Index in non IUGR and IUGR groups

non IUZR group (Me = 71.6, IQR = 60.5 to 72.8). There is a statistically significant difference in median value of FL between these two groups, U = 1248.000, z = - 2.904, p = 0.004.

Fetuses in IUZR group had lower median value of BPD (Me = 84.6 mm, IQR = 80.0 to 86.4) compared to non IUZR group (Me = 92.4 mm, IQR = 82.3 to 93.5). There is a statistically significant difference in median value of BPD between these two groups, U = 884.000, z = - 4.817, p < 0.001. Fetuses in IUZR group had lower median value of AFI (Me = 6.5 cm, IQR = 4.5 to 11.0) compared to non IUZR group (Me = 14.3 cm, IQR = 12.3 to 15.7).

There is a statistically significant difference in median value of AFI between these two groups, U = 334.500, z = -7.696, p < 0.001. Median of body mass of newborns in IUGR group was 2 220 g (IQR = 2 055 to 2 350) and 3 200 g (IQR = 2 615 to 3 487.5) in non IUGR group. There was a statistically significant difference, U = 1 065.500, z = -3.856, p < 0.001. HCI is calculated as ratio of FLL / BPD. Fetuses in IUZR group had lower median value of HCI (Me = 0.5, IQR = 0.49 do 0.51) compared to non IUZR group (Me = 0.59, IQR = 0.54 do 0.60). There is statistically significant difference in median value of HCI between these two groups, U = 115.000, z = - 8.860, p< 0.001 (Figure 4).

4. DISCUSSION

In this prospective study, we evaluated ultrasound fetoplacental parameters in fetuses with IUGR and non IUGR and we calculated HCI as a new parameter of IUGR. In our study, fetuses in IUZR group had significantly lower median value of FLL, FL, BPD and AFI compared to non IUZR group. We calculated HCI as ratio of FLL an BPD and we concluded that fetuses in IUZR group had lower median value of HCI compared to non IUZR group. In the study Stephens AS et al., it is determined brain to liver weight ratio (BLWR) thresholds for IUGR using autopsy. The BLWR ranged from 1.02 to 7.30 and was positively associated with IUGR (18). Bhimarao et al., are compared the accuracy of transcerebellar diameter/abdominal circumference with head circumference/abdominal circumference in predicting asymmetric intrauterine growth retardation after 20 weeks of gestation. BPD, HC, AC and FL along with transcerebellar diameter (TCD) were measured for assessing the sonological gestational age. They concluded that TCD/AC ratio had a better diagnostic validity and accuracy compared to HC/AC ratio in predicting asymmetric IUGR (19). Increased TCD/AC values are suspicious of fetal growth restriction and may be useful in the early detection of fetal IUGR (20, 21). In the study of Vermeer N and Bekker MN, an isolated short femur is associated with intrauterine growth restriction and adverse pregnancy outcome (22). De Carvalho AA et al., are investigated the association between the mid trimester presence of short femur and short humerus and intrauterine growth restriction. Short femur [odds ratio = 9.7, 95% confidence interval = 1.9-50.2, p = 0.03] and short humerus (odds ratio = 13, 95% confidence interval = 4.9-34.6, p < 0.001) were associated with fetal growth restriction (23). The diagnostic approach to IUGR should integrate information from maternal history and physical examination with information from sonographic evaluation of the fetus, placenta, and amniotic fluid.

5. CONCLUSION

In a fetus with IUGR in preeclampsia there is a reduction in FLL, FL, BPD, AFI and HCI and there is a early maturation of the placenta. By measurement of fetoplacental ultrasonic parameters of liver, pregnant women will experience prediction of risk pregnancy (preeclampsia with IUGR) due to hypoxia so that timely access and adequate therapy can reduce rates of perinatal morbidity, mortality, preventing growth restriction, to reduce the incidence of mental retardation and neurological disorders in newborns.

- **Author's contribution:** author and all co-authors of this paper have contributed in all phases if it's preparing. Final proof reading was made by first author.
- **Conflict of interest:** none declared.

- **Definition of abbreviations:** IUGR = Intrauterine growth restriction; FLL = Fetal Liver Length; FL = Femur Length; BPD = Biparietal diameter; AFI = Amniotic Fluid Index.

REFERENCES

1. Carberry AE, Gordon A, Bond DM. et al. Customised versus population-based growth charts as a screening tool for detecting small for gestational age infants in low-risk pregnant women. Cohraine Database Syst Rev. 2014; 5: CD008549.

2. Harding K, Evans S, Newnham J. Screening for the small fetus: a study of the relative efficacies of ultrasound biometry and symphysiofundal height. Aust N Z J Obstet Gynaecol. 1995; 35: 160.
3. Duncan KR, Issa B, Moore R, et al. A comparison of fetal organ measurements by echo-planar magnetic resonance imaging and ultrasound. BJOG. 2005; 112: 43.
4. American College of Obstetricians and Gynecologists. ACOG Practice bulletin no. 134: fetal growth restriction. Obstet Gynecol. 2013; 121: 1122.
5. World Health Organization. WHO report: reducing risks, promoting healthy life. Geneva, Switzerland, World Health Organization, 2002.
6. Chang TC, Robson SC, Boys RJ, Spencer JA. Prediction of the small for gestational age infant: which ultrasonic measurement is best? Obstet Gynecol. 1992; 80: 1030.
7. Owen P, Khan KS, Howie P. Single and serial estimates of amniotic fluid volume and umbilical artery resistance in the prediction of intrauterine growth restriction. Ultrasound Obstet Gynecol. 1999; 13: 415.
8. Warsof SL, Cooper DJ, Little D, Campbell S. Routine ultrasound screening for antenatal detection of intrauterine growth retardation. Obstet Gynecol. 1986; 67: 33.
9. Chambers SE, Hoskins PR, Haddad NG, et al. A comparison of fetal abdominal circumference measurements and Doppler ultrasound in the prediction of small-for-dates babies and fetal compromise. Br J Obstet Gynaecol. 1989; 96: 803.
10. Roberts AB, Mitchell JM, McCowan LM, Barker S. Ultrasonographic measurement of liver length in the small-for-gestational-age fetus. Am J Obstet Gynecol. 1999; 180: 634.
11. Senoh D, Hata T, Kitao M. Fetal liver length measurement does not provide a superior means for prediction of a small for gestational age fetus. Am J Perinatol. 1994; 11: 344.
12. Campbell S, Wilkin D. Ultrasonic measurement of fetal abdomen circumference in the estimation of fetal weight. Br J Obstet Gynaecol. 1975; 82: 689.
13. Shepard MJ, Richards VA, Berkowitz RL, et al. An evaluation of two equations for predicting fetal weight by ultrasound. Am J Obstet Gynecol. 1982; 142: 47.
14. Ott WJ, Doyle S, Flamm S, Wittman J. Accurate ultrasonic estimation of fetal weight. Prospective analysis of new ultrasonic formulas. Am J Perinatol. 1986; 3: 307.
15. Vintzileos AM, Campbell WA, Rodis JF, et al. Fetal weight estimation formulas with head, abdominal, femur, and thigh circumference measurements. Am J Obstet Gynecol. 1987; 157: 410.
16. Hadlock FP. Evaluation of fetal weight estimation procedures. In: Quantitative Obstetrical Ultrasonography, Deter RL (Ed), Wiley Medical, New York, 1986.
17. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. Obstet Gynecol. 2013; 122: 1122.
18. Stephens AS, Bentley JP, Taylor LK, Arbuckle SM. Diagnosis of fetal growth restriction in perinatal deaths using brain to liver weight ratios. Pathology. 2015 Jan; 47(1): 51-7.
19. Bhimarao, Nagaraju RM, Bhat V, Gowda PV. Efficacy of Transcerebellar Diameter/Abdominal Circumference Versus Head Circumference/Abdominal Circumference in Predicting Asymmetric Intrauterine Growth Retardation. JCDR. 2015; 9(10): TC01-TC05.
20. Vinkensteijn AS, Mulder PG, Wladimiroff JW. Fetal transverse cerebellar diameter measurements in normal and reduced fetal growth. Ultrasound Obstet Gynecol. 2000;15(1): 47-51.
21. Khan N, Chaudhri R, Nazir T. Role of Transverse Cerebellar Diameter in Diagnosis of Asymmetrical Fetal Growth Restriction. JRMC. 2013; 17(2): 231-33.
22. Vermeer N, Bekker MN. Association of isolated short fetal femur with intrauterine growth restriction. Prenat Diagn. 2013 Apr; 33(4): 365-70.
23. de Carvalho AA, Carvalho JA, Figueiredo I Jr, Velarde LG, Marchiori E. Association of midtrimester short femur and short humerus with fetal growth restriction. Prenat Diagn. 2013 Feb; 33(2): 130-3.