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Assessment of Accuracy of Three Ultrasound Methods for Prediction of Intrauterine Growth Restriction

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ABSTRACT

Background: fetal growth restriction (FGR) is one of the most important complications encountered during pregnancy**.** The growth-restricted fetus is a fetus that fails to reach its growth potential and is at risk for adverse perinatal morbidity and mortality. The American College of Obstetricians and Gynecologists (ACOG) defines an IUGR fetus as a fetus with an estimated weight below the 10th percentile

Objective: the study aimed to assess accuracy of transcerebellar diameter (TCD)/ abdominal circumference (AC) ratio, head circumference (HC)/ abdominal circumference (AC) ratio and hepato-cephalic index (HCI) in predicting intrauterine growth restriction (IUGR) after 20 weeks of gestation in pregnant women at risk of developing IUGR.

Materials and Methods: a prospective nested cohort study was conducted on 77 pregnant women at risk for IUGR at Ain-Shams University Maternity hospital. all women were examined by abdominal two-dimensional ultrasound after 20 weeks of gestation to assess the sonographic gestational age (BPD, HC, FL, AC, AFI, degree of placental maturation) in fetuses. The Fetal Liver Length (FLL) and Transcelebellar Diameter (TCD) were measured at the time of the scan. Hepato-cephalic index (HCI) was calculated as Fetal Liver Length (FLL)/ Biparital diameter (BPD). TCD/AC ratio was calculated by dividing Transcerebellar diameter (TCD) and abdominal circumference (AC). HC/AC ratio was calculated by dividing Head circumference (HC) and abdominal circumference (AC). All women were followed up and an abdominal ultrasound was done after 3 weeks to confirm diagnosis of IUGR and the same fetal parameters were measured and documented

Results: in predicting IUGR; **TCD/AC** and **HC/AC** have significant excellent diagnostic performance with 95%CI 0.829–1.000 and 0.851–0.974 respectively. **HCI** has significant moderate diagnostic performance with 95% CI 0.787–0.956. As regards comparison between the three ratios in prediction of IUGR in our study, we found that: **TCD/AC with a cut-off value ≥13.77** has the highest diagnostic performance in prediction of IUGR. **HC/AC with a cut-off value ≥1.04** has moderate diagnostic characteristics in prediction of IUGR. **HCI with a cut-off value ≤0.55** has the lowest diagnostic characteristics in prediction of IUGR

Conclusions: TCD/AC ratio had a better diagnostic validity and accuracy compared to HC/AC and HCI in predicting IUGR.

Keywords: Intrauterine growth restriction , transcerebellar diameter, head circumference, abdominal circumference.

INTRODUCTION

Fetal growth restriction (FGR) is one of most important complications encountered during pregnancy [(1)]. The terms small for gestational age (SGA) and Intrauterine growth restriction (IUGR) are often used interchangeably, although this is misleading. The growth-restricted fetus is a fetus that fails to reach its growth potential and is at risk for adverse perinatal morbidity and mortality. The American College of Obstetricians and Gynecologists (ACOG) defines an IUGR fetus as a fetus with an estimated weight below the 10th percentile [(2)]. But not all fetuses measuring less than the 10th percentile are at risk for adverse perinatal outcome; many are just constitutionally small.

IUGR refers to the fetus who is SGA and displays other signs of chronic hypoxia or malnutrition. SGA is defined here as a fetus who measures less than the 10th percentile for gestational age, whether it be because he is growth-restricted (IUGR) or just constitutionally small [(3)]. Approximately, 70% of fetuses is classified as being below the tenth percentile due to constitutional factors, such as female sex and ethnicity of the parents, and are not, therefore, involved in factors that can determine increased perinatal morbidity and mortality [(4)].

IUGR is estimated to affect approximately 3%–5% of pregnancies, depending on the population

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examined [5]. After prematurity, IUGR is the second largest cause of perinatal mortality [6]. Poor fetal growth is associated with severe disability [7], significant but subtle impairments in motor and cognitive function and poor general health in later life, possibly related to programming of the autonomic nervous system [8].

Sonographic fetal parameters are routinely measured both to predict gestational age and to manage pregnancies with fetuses who have growth disturbances [9]. Ultrasound biometry of the fetus is now the gold standard for assessing fetal growth [10]. Multiple tools have been developed to allow the attending physician to prenatally assess the likelihood of IUGR using biometric measurements. In order of increasing complexity, these include cross-sectional growth charts**,** estimated fetal weight (EFW) and related charts [11]. customized growth charts [12]. and conditional growth charts for longitudinal assessment [13]. Several diameters and circumferences have been studied concerning their correlation to the true gestational age such as biparietal diameter (BPD), femur length (FL), head circumference (HC) and abdominal circumference (AC) [14].

The transcerebellar diameter (TCD) has been one of the most reliable ultrasound parameters for growth. The TCD was the shown to be a reliable parameter that is significantly correlated with gestational age [15]. Fetal abdominal circumference (AC) is the parameter that is affected first during impaired fetal growth. It is the most sensitive single morphometric indicator of FGR [16]. Although it is not fully functional, fetal liver plays a critical role in glucose, fat metabolism, and hematopoiesis during fetal development. It has both endocrine and metabolic functions. In this manner, fetal problems may affect fetal liver development even at early stages of the fetal development [17]. Measurement of fetal hepatic length to identify fetal growth restriction is of interest, since the fetus has severely depleted hepatic glycogen stores associated with growth restriction [18].

AIM OF THE STUDY

The study aims to assess accuracy of transcerebellar diameter (TCD)/abdominal circumference (AC) ratio, head circumference (HC)/ abdominal circumference (AC) ratio and hepato-cephalic index (HCI) in predicting intrauterine growth restriction (IUGR) in pregnant women at risk of developing IUGR.

PATIENTS AND METHODS

A prospective nested cohort study was conducted on 77 pregnant women at risk for IUGR at Ain-Shams University Maternity hospital. Women recruited in the study after written informed consent in Arabic language. Patients were selected according to the following **inclusion criteria**: Any female in reproductive age. Patients with regular cycles, has 1sttrimesteric ultrasound confirming the gestational age, Gestational age: After 20 weeks gestation, Singleton pregnancy. Pregnant women at risk for intrauterine growth restriction (IUGR): Preeclampsia, Diabetes, Cyanotic heart disease, systemic lupus erthromatosis (SLE), antiphospholipid syndrome (APS), previous history of IUGR. **Exclusion criteria**: Patients with irregular cycles or unsure of dates or cannot confirm the gestational age, Multiple gestation, Congenital fetal malformations.

METHODS

After recruitment and consenting all women were subjected to full history taking, dating of pregnancy, and general examination, initially; all women were examined by abdominal two dimensional ultrasound after 20 weeks of gestation to assess the sonographic gestational age (BPD, HC, FL, AC, AFI, degree of placental maturation) in fetuses. The Fetal Liver Length (FLL) and Transcelebellar Diameter (TCD) were measured at the time of the scan. The Cerebellar View was obtained by rotating the transducer in the axial plane centred on the thalamus to show the cerebellar hemispheres. This view shows the cerebellum, the cisterna magna, the cavum septipellucidi and frequently, the anterior horns of the lateral ventricles. The transcerebellar diameter (TCD) was measured as the maximum transverse diameter in this mentioned plane. Sonographic measurement of the fetal liver length (FLL) was performed using the following technique, First, the fetal aorta was identified in a longitudinal plane; the transducer then was moved parallel to this plane until both the right hemidiaphragm and the tip of the right lobe of fetal liver were visualized. Finally, the FLL was measured from the top of the right hemidiaphragm to the tip of the right lobe, Hepato-cephalic index (HCI) was calculated as Fetal Liver Length (FLL)/ Biparital diameter (BPD). TCD/AC ratio was calculated by dividing Transcerebellar diameter (TCD) and abdominal circumference (AC). HC/AC ratio was calculated by dividing Head circumference (HC) and abdominal circumference

(AC). All women were followed up and an abdominal ultrasound was done after 3 weeks to confirm diagnosis of IUGR and the same fetal parameters were measured and documented. The ultrasound apparartus was Samsung H60 with a convex abdominal probe of (2-6) MHz.

The study was approved by ethical committee of Obstetrics and Gynecology department, Ain Shams University.

Statistical analysis

The collected data were coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 22.0, IBM Corp., Chicago, USA, 2013. Descriptive statistics were done for quantitative data as minimum& maximum of the range as well as mean±SD (standard deviation) for quantitative normally distributed data, while it was done for qualitative data as number and percentage. Inferential analyses were done for quantitative variables using independent t-test in cases of two independent groups with normally distributed data.

In qualitative data, inferential analyses for independent variables were done using Chi square test for differences between proportions and Fisher's Exact test for variables with small expected numbers. ROC curve was used to evaluate the performance of different tests differentiate between certain groups. The level of significance was taken at P value < 0.050 is significant, highly significant at P value < 0.01, otherwise is non-significant.

RESULTS

Total of 77 pregnant women at high risk for IUGR after 20 weeks gestation were enrolled to the study, 2 cases were dropped out due to loss of contact with them. Finally, 75 pregnant women at risk for IUGR were divided into two groups according to the results:

Group I: 29 pregnant women with IUGR.

Group II: 46 pregnant women without IUGR.

Table (1): Show basal US findings among the studied cases

Variables		**Mean±SD**	**Range**
GA (weeks)		31.5±3.8	22.1–37.4
GA (days)		220.5±26.9	155.0–262.0
TCD (cm)		3.5±0.5	2.3–4.7
AC (cm)		25.4±3.7	16.7–34.3
HC (cm)		24.4±4.2	14.7–35.9
FLL (cm)		4.3±0.5	3.0–5.3
BPD (cm)		7.9±1.0	4.7–9.5
FL (cm)		5.8±0.8	3.6–8.0
EFW (g)		1473.3±635.6	569.0–3037.0
AFI (cm)		9.6±2.8	4.3–15.7
TCD/AC		13.77±0.22	13.36–14.81
HC/AC		1.05±0.05	0.94–1.23
FLL/BPD(HCI)		0.55±0.03	0.42–0.59
Placntal maturation	**Grade I**	19	24.7
	Grade II	44	57.1
	Grade III	14	18.2

Table (2): Show follow up US findings among the studied cases

Variables		Mean±SD	Range
GA (weeks)		33.5±3.5	23.1–40.0
GA (days)		234.8±24.6	162.0–280.0
TCD (cm)		3.9±0.5	2.6–5.0
AC (cm)		27.7±3.9	17.3–36.6
HC (cm)		26.0±4.9	14.3–38.1
FLL (cm)		4.6±0.5	3.1–5.7
BPD (cm)		8.5±0.8	6.2–9.7
FL (cm)		6.3±0.7	4.0–8.3
EFW (g)		1631.4±651.6	630.0–3160.0
AFI (cm)		9.5±2.9	3.9–15.2
TCD/AC		14.24±0.59	13.62–15.12
HC/AC		1.08±0.06	0.94–1.22
FLL/BPD (HCI)		0.54±0.04	0.40–0.60
Placntal maturation	**Grade I**	7	9.1
	Grade II	25	32.5
	Grade III	45	58.4

Table (3): show the cases ofIUGR among the studied cases

IUGR	N	%
Present (G1)	29	38.7
Absent (G2)	46	61.3

Table (4): Comparison between Group I (IUGR) and Group II (non-IUGR) cases regarding follow up US findings

Variables	G1 (IUGR) (N=29)	G2 (Non-IUGR) (N=46)	P	Significance
GA (weeks)	33.2±3.1	33.8±3.8	0.464	-
GA (days)	232.3±21.5	236.5±26.6	0.464	-
TCD (cm)	3.8±0.4	4.0±0.5	0.067	NS
AC (cm)	25.6±2.7	29.2±3.9	**<0.001***	**HS**
HC (cm)	22.5±2.8	28.5±4.6	**<0.001***	**HS**
FLL (cm)	4.3±0.4	4.8±0.5	**<0.001***	**HS**
BPD (cm)	8.7±0.7	8.4±0.9	0.068	NS
FL (cm)	6.1±0.5	6.4±0.8	**0.020***	**S**
EFW (g)	1383.2±382.7	1798.7±740.5	**0.002***	**HS**
AFI (cm)	7.1±2.2	11.2±2.0	**<0.001***	**HS**
TCD/AC	14.94±0.09	13.76±0.08	**<0.001***	**HS**
HC/AC	1.14±0.04	1.04±0.03	**<0.001***	**HS**
FLL/BPD (HCI)	0.49±0.03	0.57±0.02	**<0.001***	**HS**
Pl. Grade I	16 (34.8%)	5 (10.9%)	**<0.001***	**HS**
Pl. Grade II	21 (45.7%)	22 (47.8%)		
Pl. Grade III	9 (19.6%)	19 (41.3%)		

^Independent t-test, &Fisher's Exact test, *Significant, S Significant, HS Highly significant, NS Non-significant.

Table (4) show that: Cases with IUGR had significant lower follow up **AC, EFW, FLL, AFI, FLI/BPD (HCI) and placental maturation**, as well as significantly higher **HC, TCD/AC and HC/AC.**

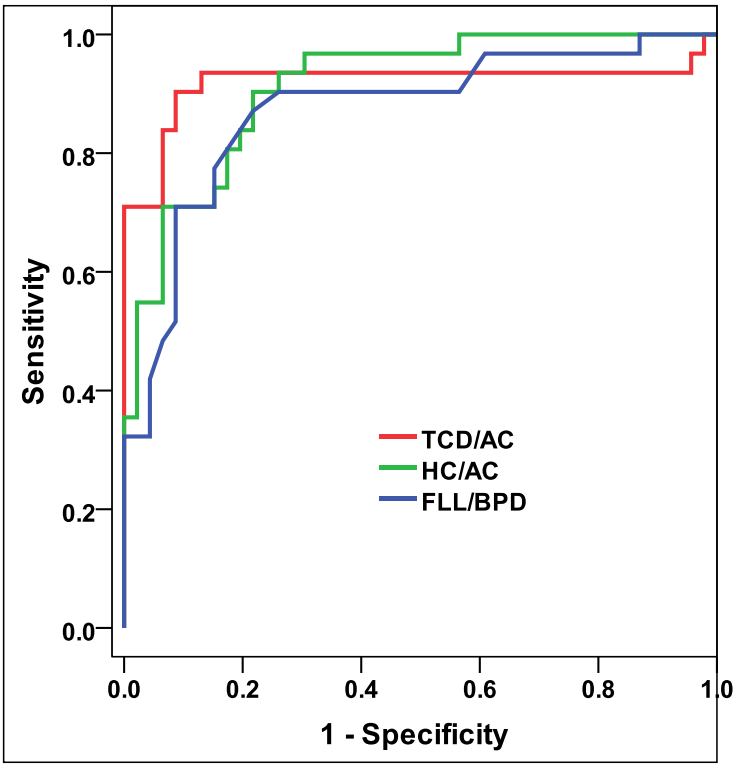

Figure (1): ROC curve for diagnostic performance of TCD/AC, HC/AC and FLL/BPD (HCI) in prediction of IUGR among studied cases.

Basal US TCD/AC ≥13.77 had high diagnostic characteristics in prediction of IUGR**.**
Basal US HC/AC ≥1.04 had moderate diagnostic characteristics in prediction of IUGR.
Basal US FLL/BPD (HCI) ≤0.55 had moderate diagnostic characteristics in prediction of IUGR.

DISCUSSION

Ultrasound shows more promise than any other clinical parameter for prediction of gestational age in growth restricted fetuses. Different kind of biometric measurements have been evaluated alone or in combination including BPD, HC, AC, FL. Some of these nontraditional ultrasound measurements are TCD and FLL [19].

Many studies have shown that TCD/AC ratio is a stable, gestational age independent parameter after 20 weeks of gestation. Increased TCD/AC values are suspicious of fetal growth restriction and may be useful in the early detection of fetal IUGR[20].

In general, the fetal liver is the earliest and most severely affected organ in fetal growth abnormalities. The direct ultrasonographic measurement of the fetal liver adds another parameter that could be used in the evaluation of early stages of abnormal fetal growth. The rapid growth of the fetal liver length during third trimester offers a distinct advantage for early detection FGR as the growth rate of the other fetal parameters (BPD, HC, AC, FL) decreases considerably [21].

In this study, 75 pregnant women were divided into two groups:

Group I: 29 pregnant women with IUGR.

Group II: 46 pregnant women without IUGR. There is a statistically insignificant difference between Group I and Group II regarding TCD suggesting that it is unaffected by fetal growth changes thus TCD serves as age independent parameter.

There is also significant decrease in FLL and HCI**,** as well as significant increase in HC**,** TCD/AC and HC/ACbetween Group I and Group II. In our study in predicting IUGR; **TCD/AC** and **HC/AC** have significant excellent diagnostic performance with 95%CI 0.829–1.000 and 0.851–0.974 respectively.

HCI has significant moderate diagnostic performance with 95% CI 0.787–0.956. As regards comparison between the three ratios in prediction of

IUGR in our study, we found that: **TCD/AC with a cut-off value ≥13.77** has the highest diagnostic performance in prediction of IUGR with Sensitivity and Specificity of 93.5% and 87% respectively, with Positive Predictive value (PPV) of 82.9%, Negative Predictive value (NPV) of 95.2%and overall diagnostic accuracy of 89.6%.

HC/AC with a cut-off value ≥1.04 has moderate diagnostic characteristics in prediction of IUGR with sensitivity and specificity of 90.3% and 78.3% respectively, with Positive Predictive value (PPV) of 73.7%, Negative Predictive value (NPV) of 92.3% and overall diagnostic accuracy of 83.1%. **HCI with a cut-off value ≤0.55** has the lowest diagnostic characteristics in prediction of IUGR with sensitivity and specificity of 90.3% and 68.9% respectively, with Positive Predictive value (PPV) of 66.7%, Negative Predictive value (NPV) of 91.4% and overall diagnostic accuracy of 77.9%.

As regards TCD/AC in prediction of IUGR, our results were in agreement with *Bhimarao et al.* [22] who stated that TCD/AC ratio was an age independent parameter that was used in diagnosis of IUGR with sensitivity of 88%, specificity of 93.5% and cut off value of ≥13.63 for prediction of FGR. *Khan et al.* [23] in their study which involved 30 high risk patients with known accurate gestational age and singleton pregnancy, found that raised TCD/AC ratio was observed in 15 patients out of 30 (50%) with cut off value of 16.03 for predicting FGR giving the sensitivity, specificity of 77.78% and 83.34% respectively which was very close to our results. *Chawanpaiboon et al.* [24] compared the mean TCD/AC ratio between fetuses with and without IUGR, finding that it was significantly higher in fetuses with IUGR (P<0.001) which is in agreement of our results.

As regards HC/AC in prediction of IUGR, *Toyama et al.* [25] were in agreement with our results as in their retrospective study on 177 neonates who had undergone prenatal ultrasonography to evaluate abnormalities detected by primary screening found that significant elevation of HC/AC ratio ($p < 0.001$) among SGA neonates with cut-off value of 1.15 predicting SGA at birth regardless the gestational age at the time of scan with sensitivity of 70% and specificity 65%.

Ott [26] evaluated a number of fetal parameters including HC/AC ratio for prediction of IUGR in 501 pregnant women at increased risk for IUGR and stated that HC/AC ratio was fair in prediction of IUGR with sensitivity of 49.1%, specificity of 83.7%, PPV of 47.1% and NPV of 84.8% which is close to our results.

As regards HCI in prediction of IUGR, *Dacaj et al.* [27] studied 120 pregnant women divided in two groups: non IUGR group included healthy pregnant women *(n=60)* and IUGR group included pregnant women with preeclampsia *(n=60)* and found that There is statistically significant difference in values of HCI ($p < 0.001$) between these two groups which is in agreement with our results. They also found a statistically significant difference in values of FLL ($p < 0.001$) between the two groups which is in agreement with our results.

CONCLUSION

We concluded that the three ratios (TCD/AC, HC/AC, and HCI) are of great value for prediction of IUGR after 20 weeks of gestation. However, TCD/AC ratio had a better diagnostic validity and accuracy compared to HC/AC and HCI in predicting IUGR.

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