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Efficacy of Transcerebellar diameter/ Abdominal circumference Versus Head circumference/ Abdominal circumference in predicting Asymmetric Intrauterine Growth Retardation

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Abstract: Accurate gestational dating is of paramount importance and the cornerstone for management of pregnancies, easily reproducible sonographic fetal biometric parameters for gestational dating are clinically important for the optimal obstetric management of pregnancies. This is especially true in determining timing of a variety of gestational tests, assessing adequacy of growth and timing of delivery for the optimal obstetric outcome. As Determination of fetal age and growth is crucial in planning pregnancy management, especially for low-birth-weight infants, Ultrasound screened and managed pregnancies with low-birth-weight babies reduce the mortality rate by 60%. Fetal age and growth are assessed by crown-rump length during the 5th to 10th weeks of gestation. After that, a combination of measurement including the biparietal (BPD) diameter of the skull, Femur length and abdominal circumference are used. IUGR is caused mostly by asphyxia and reduced uteroplacental blood flow. In acute asphyxia, cerebellar blood flow remains unchanged as a consequence of redistribution of cardiac output. The blood flow shifts mainly to the central parts including the brain, heart and adrenal glands. In humans, cerebellar growth may be least affected by IUGR, therefore TCD measurement is mostly accurate in prediction of gestational age and so IUGR. The transverse cerebellar diameter (TCD) has been one of the most reliable ultrasound parameters for growth especially early gestation. The TCD was the only parameter that correlated with gestational age by the end of the second trimester ***(Pinar et al., 2002).*** The aim of the study is to evaluate the accuracy, usefulness and efficacy of TCD/AC versus HC/AC in singleton pregnancies as a reliable predictor of GA in fetuses with IUGR after 20 weeks of gestation by ultrasound. This cross-sectional study was conducted on 50 pregnant women diagnosed as IUGR at El-Zahraa University hospital (outpatient clinic), the transcerebellar diameter, the biparietal diameter, the head circumference, the abdominal circumference and the femur length were measured for determination of gestational age and so assessing the efficacy of TCD/AC in predicting asymmetric IUGR. The mean age of the study population was 25.8 years, while the mean gestational age by the LMP was 30.7, by the TCD was 29.9, by HC was 28.8, by AC was 26.1, by TCD/AC was 13.74 and by HC/AC was 1.04.
[Asmaa Mahmoud Abd El-Wahab, Hend Salah and Dina Mahmoud Gamal Mohamed Elboghdady. **Efficacy of Transcerebellar diameter/ Abdominal circumference Versus Head circumference / Abdominal circumference in predicting Asymmetric Intrauterine Growth Retardation.** *Nat Sci* 2020;18(2):109-116]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). http://www.sciencepub.net/nature. 17. doi:10.7537/marsnsj180220.17.

Keywords: Efficacy; Transcerebellar; diameter; Abdominal circumference; Versus; Head; circumference; Abdominal circumference; predicting; Asymmetric; Intrauterine; Retardation

1. Introduction

The estimation of pregnancy dates is important for the mother, who wants to know when to expect the birth of her baby, and for her health care provider, so they may choose the way in which to perform various screening tests and assessments. Accurate gestational dating is one of the most important assessments obstetrical providers make in pregnancy, given that all of the various management strategies are dependent on knowing where the patient is in gestation. In addition to traditional biometry, ancillary biometric and non-biometric measurements can help narrow the biologic variability between fetuses. Moreover, one can employ these non-traditional measurements both in late gestation to assist in determining appropriate gestational age and fetal lung maturity, and in other specific clinical situations, such as oligohydramnios, in which compression of the fetal head and abdomen can lead to difficulty in obtaining an accurate biparietal diameter and abdominal circumference **(Amy and Henry, 2008).**

Since the beginning of ultrasound fetal measurements, the possibility of population differences has been considered (**Cummings, 1982**). Some researchers have suggested that population differences in fetal biometry are negligible and that separate standards are not essential (**Campbell et al., 1991**).

Mounting evidence shows that the fetal cerebellum exhibits a progressive growth throughout the gestation period (**Malik and Waqar, 2006, Araújo et al., 2007**), so it is an organ capable of providing information on the prediction of gestational age during the pregnancy. Although there are ultrasound studies regarding the correlation between transverse cerebellar diameter (TCD) in fetuses and gestational age, most of them address the third trimester of pregnancy or short gestational periods (**Vinkesteijn et al., 2000, Chang et al., 2000, Chavez and Ananth, 2003, Malik and Waqar, 2006**). Therefore, it is important to study the correlation between fetal TCD and pregnancy age addressing longer and earlier gestational periods.

The transverse cerebellar diameter (TCD) has been one of the most reliable ultrasound parameters for growth. The TCD was the only parameter that correlated with gestational age by the end of the second trimester (**Pinar et al., 2002**).

There is relative preservation of normal cerebellar growth in growth-restricted fetuses and a similar rate of growth in singleton and multifetal gestations. The transverse cerebellar diameter therefore represents an independent biometric parameter that can be used in both singleton and multifetal pregnancies to assess normal and deviant fetal growth (**Goldstein and Albert, 1995**).

Small for gestational age (SGA) is defined as an estimated fetal weight or abdominal circumference less than 10^{th} centile **(RCOG,2013).**

Fetal growth restriction is not synonymous with SGA.

Some, but not all, SGA are growth restricted fetuses while 50-70% of SGA fetuses are constitutionally small, with fetal growth appropriate for maternal size and ethnicity **(Alberry and soothill, 2007).**

Fetal growth restriction is defined as fetuses whose growth velocity slows down or stops completely because of inadequate oxygen and nutritional supply or utilization **(Cardozo and Luckas,2010).** Low birth weight refers to an infant with a birth weight <2500gm **(RCOG,2013).**

Fetal growth restriction is a common and complex obstetric problem as this fetal condition is associated with significant perinatal morbidity and mortality **(Kramer et al., 2006).**

Fetal growth restriction is noted to affect approximately 10-15% of pregnant women **(Acog, 2012).**

The screening and diagnosis of fetal growth restriction is based on establishment of accurate dating, assessment of risk factors, followed by ultrasound for fetal growth. Accurate gestational age can be estimated by menstrual history, clinical examination and ultrasound **(Mongelli et al., 2005).** Prediction of gestational age based on sonographic fetal parameters is perhaps the cornerstone in modern obstetrics and continues to remain an important component in management of pregnancies with fetuses who have growth disturbances **(Martin et al, 2007).**

Ultrasound has been used as a tool for determining fetal health and a variety of sonographic parameters have been used to screen and diagnose fetal growth restriction including fetal biometry, fetal body proportions **(Campbell et al., 2000),** amniotic fluid volume **(Owen et al, 1999),** and estimated fetal weight by Hadlock formula as it is preferable due to its low level of systemic error **(Siemer et al, 2008).**

The four basic measurements, including biparietal diameter (BPD), head circumference (HC), femur length (FL) and abdominal circumference (AC), can be performed using standard AIUM guidelines **(AIUM,2013).**

Malik and Waqar, 2006 found that the fetal cerebellum exhibits a progressive growth throughout the gestation. So, it is an organ capable of providing information on the prediction of gestational age during pregnancy. Transcerebellar diameter (TCD) is one such fetal parameter that has remained consistently superior in predicting gestational age in both the second and third trimesters **(Chavez et al, 2004)**.

Aim of the Work

This study aims to evaluate the efficacy of TCD/ AC versus HC/AC in predicting asymmetric IUGR in singleton gestations.

Patients and Methods

1. Study design:

This cross-sectional study was conducted on 50 pregnant women diagnosed as growth restricted fetuses (IUGR) in El Zahraa university hospital (outpatient clinic) to detect the efficacy of TCD/AC versus HC/AC in predicting asymmetric IUGR.

Inclusion criteria:

– Singleton pregnancies.
– Non anomalous pregnancies.
– 20week gestation or more.
– Favorable lie to visualize posterior fossa.
– Accurately determined gestational age by LMP or first trimester US.

Exclusion criteria:

- Multiple gestation.
- Anomalous pregnancies.
- Moderate to severe polyhydramnios.
- Previous irregular menstrual cycles.
- Maternal age <18 or >35 years.
- Symmetrical IUGR.
- Doubtful or unknown last menstrual period.

Methods and operational design:

The selected cases were subjected to the following:

- Verbal consent was taken.
- Thorough history taking with emphasis on the date of the last menstrual period to ensure its reliability and assess the inclusion and exclusion criteria as follows:

-Personal history: name, age, educational level, residence, address, occupation, special habits.

-Menstrual & obstetrics history: menarche, gravidity, parity, LMP.

-Medical history of previous pregnancies and current pregnancy.

- Abdominal examination including symphysis-fundal height.
- Ultrasound to assess the following:

Fetal viability.
Biparietal diameter.
Femur length.
Abdominal circumference.
Transcerebellar diameter.
Head circumference.
7. TCD/AC.
8. HC/AC.
9. AFI.
10. placental location.

- Laboratory investigations as CBC, Bleeding Profile, Random blood sugar, renal function test, liver function test, urine analysis to detect risk factors.

Outcome measures:

Primary outcome:

- The correlation between transcerebellar diameter/Abdominal circumference, head circumference/Abdominal circumference and gestational age calculated by LMP in predicting Asymmetric IUGR.

3. Results

Table (1) shows that: Most of the antenatal women were in the age group of 19-33 years with Mean±**SD** 25.8±3.0 years.

Regarding parity of our studied cases, most of them were PG up to P4 with gestational age after 20 weeks, mostly between 25-36 weeks, calculated with LMP in patients with regular cycles with **Mean±SD** 30.7±2.8. IUGR usually occurs to patients with medical disorders whether in previous pregnancies or in the current one, 8% of cases were associated with previous history of IUGR, 44% of cases with anaemia, 12% with Hypertension, 8% with DM and 8% were smokers.

Table (1): Demographic characteristics and clinical history of the studied cases

Variables	Mean±SD	Range
Age (years)	25.8±3.0	19.0–33.0
GA (weeks)	30.7±2.8	25.0–36.0
Smoking	4	8%

	N	%
Previous history of IUGR	4	8.0
Anemia	22	44.0
Hypertensive disorders	6	12.0
DM	4	8.0
Malnutrition	5	10

Parity	N	%
PG	**8**	**16**
P1	**15**	**30**
P2	**12**	**24**
P3	**7**	**14**
P4	**8**	**16**

Total=50

Table (2): Laboratory findings of the studied cases

Lab	Mean±SD	Range	Normal range
Hb (gm/dL)	10.2±1.5	9.1–12.6	10.5-14
WBC'S	8000±2000	5000-10000	4000-11000
Platelets	230.000±40.000	150000-450000	150000-400000
PT (sec)	12±0.5	11-12.5	11-13.5
PTT (sec)	66±1	63-68	60-70%
INR	1±0.1	0.9-1.1	0.8-1.1
ALT (IU/L)	28.8±7.7	15.0–39.0	Up to 30
AST (IU/L)	26.2±7.9	15.0–38.0	Up to 30
Urea (mg/dl)	11±3	8-14	5-20
Creatinine (mg/dl)	0.8±0.2	0.6-1	0.5-1.1
Fasting blood sugar **1 hr postprandial** **2 hrs posprandial**	88±15 120±8 100±9	70-105 110-145 90-130	60-95 100-129 Up to 120
	N	%	
Albumin (in urine)	8	16.0	

Total=50

Table (2) shows the laboratory investigations of the studied cases of asymmetric IUGR, and It is found that mild to moderate anaemia is noted among many cases with Hb ranges between 9.1–12.6 with **Mean±SD** 10.2±1.5, with 44% of cases diagnosed with anaemia (22 cases out of 50) which means that maternal anaemia is an important clinical condition and one of the most frequent causes that may lead to IUGR especially if moderate to severe anamia.

Proteinuria (Albuminuria) is detected in 8 cases (16% of cases) by urine dipsticks and was associated with preeclampsia and hypertension which affects fetal outcome by causing uteroplacental insufficiency and compromise of blood flow to the fetus resulting in IUGR.

Table (3) shows that: all parameters were less than normal because of fetal growth restriction (FGR). However, TCD is the least diameter that is affected by IUGR, so its measurements were equal or close to the normal measurements for gestational age because of the brain sparing effect.

There was significant decrease in AC as the size of fetal liver is reduced due to reduced glycogen store, So TCD/AC and HC/AC remain nearly constant in normal pregnancy but increase in FGR with **Mean±SD** 13.74±0.23 and 1.04±0.05 respectively.

Table (3): Ultrasound (US) findings among the studied cases

US		**Mean±SD**	**Range**
GA	**Week**	31.1±3.5	22.0–36.0
BPD (cm)	**Measure**	67±7	51–81
	Week	27.9±3.0	22.0–33.0
FL (cm)	**Measure**	52±6	39–64
	Week	26.4±2.6	21.0–29.0
AC (cm)	**Measure**	239±30	163–290
	Week	26.1±2.9	20.0–29.0
HC (cm)	**Measure**	268±28	210–311
	Week	28.8±3.1	23.0–34.0
TCD (cm)	**Measure**	37±5	27–47
	Week	29.9±2.7	24.0–35.0
TCD/AC		13.74±0.23	13.38–14.81
HC/AC		1.04±0.05	0.94–1.23
AFI		10.2±1.8	4.0–17.0

Total=50

Table (4) shows that: Gab between GA by LMP and GA by US indices; **TCD had narrowest gab, followed by HC, then BPD, then AC and widest in FL.**

Table (4): Gab between GA by LMP and GA by US indices

Gab (week) (Index-LMP)	**BPD**	**FL**	**AC**	**HC**	**TCD**
-5.0	0 (0.0%)	6 (12.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
-4.0	19 (38.0%)	6 (12.0%)	18 (36.0%)	0 (0.0%)	0 (0.0%)
-3.0	17 (34.0%)	28 (56.0%)	17 (34.0%)	18 (36.0%)	0 (0.0%)
-2.0	6 (12.0%)	5 (10.0%)	8 (16.0%)	18 (36.0%)	10 (20.0%)
-1.0	3 (6.0%)	3 (6.0%)	4 (8.0%)	6 (12.0%)	24 (48.0%)
0.0	5 (10.0%)	2 (4.0%)	3 (6.0%)	8 (16.0%)	15 (30.0%)
+1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)
Within ±1.0	8 (16.0%)	5 (10.0%)	7 (14.0%)	14 (28.0%)	40 (80.0%)

Total=50

Table (5) shows that: pearson correlation of TCD/AC and HC/AC equal 0.502 and 0.129 respectively which indicates significant correlation between TCD/AC and HC/AC and GA.

Table (5): Correlation between GA and TCD/AC & HC/AC

Index	**r**	**p**
TCD/AC	0.097	0.502
HC/AC	0.218	0.129

Total=50, Pearson correlation (p) and correlation coefficient (r).

Table (6) and figure (1) showed that: In predicting asymmetric IUGR **TCD/AC** and **HC/AC** had significant high diagnostic performance, However TCD/AC has more diagnostic accuracy than HC/AC, as **95% CI are** 0.000–1.000 and 0.835–1.000 respectively.

Cutoff value of TCD/AC and HC/AC was≥13.81 and ≥1.04 respectively which means that TCD/AC had a strong correlation with GA and of high diagnostic accuracy than HC/AC in predicting asymmetric IUGR.

Table (6): Diagnostic performance of basal US scores predicting asymmetric IUGR among studied cases

Factors	**AUC**	**SE**	**P**	**95% CI**	**Cutoff**
TCD/AC	0.882	0.077	**<0.001***	0.000–1.000	≥13.81
HC/AC	0.939	0.036	**<0.001***	0.835–1.000	≥1.04

AUC: Area under curve, SE: Standard error, CI: Confidence interval, *significant

Table (7) shows sensitivity, specificity, PPV, NPV and DA of both TCD/AC and HC/AC which were 88.2 %, 97 %, 93.8%, 94.1%,94% and 82.4%, 90.9%,82.4%, 90.9%, 88% respectively, which indicates high accuracy of TCD/AC than HC/AC in predicting asymmetric IUGR.

Table (7): Diagnostic characteristics of US TCD/AC and HC/AC in prediction of asymmetric IUGR

Characters	**TCD/AC ≥13.81**		**HC/AC≥1.04**	
	Value	**95% CI**	**Value**	**95% CI**
Sensitivity	88.2%	63.6%–98.5%	82.4%	56.6%–96.2%
Specificity	97.0%	84.2%–99.9%	90.9%	75.7%–98.1%
DA	94.0%	83.5%–98.7%	88.0%	75.7%–95.5%
Youden's index	85.2%	68.8%–100.0%	73.3%	52.7%–93.9%
PPV	93.8%	69.8%–99.8%	82.4%	56.6%–96.2%
NPV	94.1%	80.3%–99.3%	90.9%	75.7%–98.1%

CI: Confidence interval, YI: Youden's index, DA: Diagnostic accuracy, PPV: Positive Predictive value, NPV: Negative Predictive value, LR+: Positive likelihood ratio, LR-: Negative likelihood ratio, LR: Diagnostic odd.

4. Discussion

Intrauterine growth retardation (IUGR) refers to a condition in which a fetus in unable to achieve its genetically determined potential size. A fetus affected by IUGR forms as ubset of SGA. Infants. A fetus is growth restricted or small for gestational a gifts weight is below the10th percentile for gestational age (Cummings, ***1982)***.

Intrauterine growth restriction (IUGR) is an indicator of the increased risk of perinatal and long-term mortality and morbidity when compared to those born with normal growth. There is a considerable difference in the incidence of IUGR across different populations. In babies born with a birth weight less than 2500 gm, its prevalence is almost 33%. The incidence of IUGR shows a dependence on economic growth too, with a relatively lower incidence in developed countries (4-8%) as compared to that in developing countries (6%-30%) ***(Sawant, 2013).***

The average incidence of IUGR is nearly 8% in the general population. In nearly 35%-40% of the cases, IUGR is the consequence of an abnormal condition. Factors like placental insufficiency, maternal hypertension, cardiovascular disease, diabetes, infections, low socioeconomic status, previous history and preeclampsia are some of the known risk factors for IUGR **(Peleg, 1998).**

Poor pregnancy outcome has shown a strong link with IUGR; more than half the stillbirths are associated with IUGR and nearly 10% of perinatal mortality is consequent to undetected IUGR ***(Bernstein, 1997).***

For the fetus, the placenta is the only nutritional support available. During IUGR, the ability of the placenta to provide adequate nutrition to the fetus is restricted, thus resulting in developmental problems ***(Robinson et al,2010)***.

The maintenance of good utero-placental circulation is necessary to continue a normal pregnancy. The progression of pregnancy is marked by a number of changes and adaptations in the maternal, placental and fetal vasculatures ***(Khanduri, S., et al, 2017).***

Early identification and prediction of IUGR, to a great extent, rests in an ability to evaluate the maternal, placental and fetal vascular patterns effectively and efficiently ***(Simanaviciute D, 2006).***

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, and FL. Some of these nontraditional ultrasound measurements is TCD ***(Gottlieb and Galan 2008)***.

The transcerebellar diameter (TCD) is a measurement in posterior cranial fossa which is relatively resistant to external compression due to its strong bony walls. It is also less affected than the head circumference suggesting a preferential mechanism in the preservation of cerebellar growth relative to other cerebral structures (***Behrman, 1970).***

In a normally developing fetus the TCD increases with advancing gestational age. Several studies demonstrated good correlation between TCD and AC ***(Campbell, 1991)***. Many studies have shown that TCD/AC ratio is a stable, gestational age independent parameter after 20 weeks of gestation (***Campbell, 1994)***. Increased TCD/AC values are suspicious of fetal growth restriction ***(Khan, 2013)*** and may be useful in the early detection of fetal IUGR. It can be used to calculate gestational age in IUGR cases with better accuracy ***(Dilmen, 1996).***

In this study 50 antenatal women were selected after fulfilling the inclusion and exclusion criteria.

Risk factors associated with present pregnancy were preeclampsia in 12%, and GDM in 8%, anaemia in 44%, smoking in 8% and previous history of IUGR in 8%.

There was significant increase in TCD among all patients with asymmetric IUGR after 20 weeks of gestation, suggesting that it was unaffected by fetal growth changes thus TCD serves as age independent parameter ***(Clin,1994).***

There was also significant increase in HC, suggesting that it was also unaffected by FGR. SO, in our study in predicting IUGR; Both TCD and HC were good diagnostic parameters in predicting IUGR.

There was significant decrease in AC in our study, as the size of fetal liver is reduced due to reduced glycogen store.

So, TCD/AC and HC/AC remain nearly constant in normal pregnancy but increase in FGR, so there was as statistically significant difference in our study and have significant excellent diagnostic performance with 95%CI 0.000–1.000and0.835–1.000 respectively.

In this study, strong correlation was noted between gestational age determined by last menstrual period and fetal TCD/AC ratio after 20 weeks (r = 0.097), similar to the study conducted by ***(Haller et al, 1995)*** I n which there was correlation between TCD/AC ratio and gestational age (r = 0.095).

In the present study, significant correlation exists between the gestational age determined by the last menstrual period and HC/AC ratio after 20 weeks (r =0.218) which was consistent to the study conducted by ***(Haller et al,1995)*** in which there was strong correlation between gestational age and HC/AC (r = 0.221).

Also, in the present study, there were good diagnostic validities for HC/AC ratio in predicting asymmetric IUGR with sensitivity 82.4% and specificity 90.0% which were close to the studies conducted by (***Benson et al,1990***), (***Divon, 1994)*** and (***Ott, 2002)***, in which the sensitivity was 82%, 66% and 49.1% and the specificity was 94%, 90% and 83.7% respectively.

In the present study, HC/AC ratio showed a good diagnostic parameter for asymmetric IUGR with PPV 82.4% and NPV 90.9 % which was in correlation with the studies conducted by (***meyer et al 1995)*** and (***Ott WJ, 2002),*** that showed that HC/AC ratio was a good diagnostic parameter for IUGR with PPV 75.6% and 47.1% and NPV 69% and 84.8% respectively.

In the current study, the pearson correlation between GA & TCD was 0.502 with p-value of <0.001 which is slightly close to the study conducted by (***Bansal, et al.* 2014),** that was involving 650 pregnant patients between 14 to 40 weeks and found that TCD (mm) was equivalent to GA of fetus and the Karl Pearson correlation between GA & TCD was 0.972 with p-value of <0.001 (highly significant).

The present study shows a statistically significant difference between the mean AC in our patients with asymmetric IUGR and the measurements supposed to be in their gestational age. This again proves that in FGR, the AC will be affected more as the liver size is reduced due to reduced glycogen store.

As regards TCD/AC in prediction of asymmetric IUGR, our results showed high diagnostic validities for TCD/AC with sensitivity 88.2% and specificity 97.0% which was in agreement with (***Bhimarao et al, 2015)*** and (***meyer et al 1995)*** who stated that TCD/AC ratio was an age independent parameter that can be used in diagnosis of asymmetric IUGR with sensitivity 88%, and 83.9% and specificity 93.5 and 96.2% respectively.

For prediction of FGR. Also, ***Khan NA et al 2013***, 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 sensitivity, specificity of 77.78% and 83.34% respectively which was close to our results.

In this study the mean TCD/AC ratio after 20 weeks was taken as cut-off value for diagnosing FGR. Here, the TCD/AC ratio was≥13.81 which was close to the study of ***(Malik, 2006)*** in which the TCD/AC ratio was 14.06 +_0.59. Also, the studies conducted by ***(Meyer,1995)*** and (***Dhumale et al 2010)*** (***Bhimarao et al, 2015)*** and, (***Khan et al 2013),*** the cut-off value for fetal growth restriction were 13.68

and 13.56,13.63 and 16.03 respectively which were close to our results.

As regards HC/AC in prediction of asymmetric IUGR, in our study, HC/AC ratio cut-off value was 1.04 which was in agreement with the study conducted by (***Toyama et al 2017)*** which was done on 177 neonates who had undergone prenatal ultrasonography to evaluate abnormalities detected by primary screening and 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.

Conclusion

Both morphometric ratios TCD/AC and HC/AC were gestational age independent parameters and can be used in predicting IUGR with good diagnostic accuracy. However, TCD/AC ratio has a better diagnostic validity and accuracy compared to HC/AC ratio in predicting asymmetric IUGR.

Recommendations

Measuring the TCD as routine in the third trimester as it has the same accuracy as the current routine fetal biometry BPD & FL).

Further study focusing on assessment of the TCD in certain periods of gestations, for example; from 20-26, from 26 to 32 wks, from 32 to 36 wks and > 36 wks of gestation.

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12/17/2019