ULTRASOUND MEASUREMENT OF TRANSCEREBELLAR DIAMETER (TCD)/ABDOMINAL CIRCUMFERENCE (AC) RATIO IN NORMAL AND GROWTH RESTRICTED FETUSES ABOVE TWENTY WEEKS OF GESTATION

By

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ABSTRACT

Background: Intrauterine growth retardation (IUGR) is an obstetrical syndrome that is generally associated with increased mortality and morbidity. In IUGR, maternal placental blood flow is extremely compromised and that worsen the inter-villous circulation leading to an end-stage fetal distress.

Objective: To compare TCD/AC ratio in both normal and growth restricted fetuses in second and third trimesters and to find if there is any correlation between TCD/AC ratio and EFW.

Patients and methods: The study was conducted on 100 singleton pregnant women at EL-Sayed Galal University Hospital and Damanhour Teaching Hospital in the period between March 2019 till May 2020 and the patients were divided into two main equal groups. Group I included pregnant females with normally growing fetuses and Group II included pregnant females with growth restricted fetuses above 20 weeks of gestation.

Results: This study demonstrated the usefulness of the single cut-off value (13.75%) of the TCD/AC ratio which may contribute to the early identification of SGA infants. The problem lied in identifying the process at the onset or before the IUGR has become severe. Usually the first parameter to decrease is the fetal AC due to depletion of hepatic glycogen and subcutaneous fat stores. The TCD/AC ratio, which utilized a single cut-off value (13.75%) independent of GA, improved diagnostic sensitivity and specificity in these cases. The possible contribution of the TCD/AC ratio in identifying the fetal growth failure itself, which was more important than predicting weight at birth to be further evaluated. There was no correlation between TCD/AC ratio and EFW and no statistical significant correlation between TCD/AC ratio and UA Doppler.

Conclusion: In IUGR fetuses, the fetal TCD was less affected than fetal head circumference (HC) suggesting preferential preservation of cerebellar growth relative to other cranial structures. The TCD/AC ratio was helpful in recognizing abnormal fetal growth even when the GA was uncertain since this ratio was gestational age-independent.

Keywords: Ultrasound, Transcerebellar diameter, abdominal circumference.

INTRODUCTION

Fetal growth is defined as the time-dependent changes in the fetal body dimensions that occur throughout pregnancy. The growth rate of various parameters is rapid especially in the 1st and 2nd trimesters. They change significantly with the advancement of pregnancy and must be evaluated against normal value at that age *(Abduljalil et al., 2012)*.

Maternal adaptations to pregnancy predominate in the first trimester, while the second trimester is characterized by elaboration of placental function. Successful progression ultimately enables the fetus to reach its growth and developmental potential in the third trimester in preparation to extra-uterine life *(Baschat et al., 2010)*.

A complex and dynamic interaction of maternal, placental and fetal environment is involved in ensuring normal fetal growth *(Sankaran and Kyle, 2010)*.

The term intrauterine growth restriction has largely replaced the term IUGR. Intrauterine growth restriction means failure of the fetus to achieve its inherent growth potential. The most common definition used is fetal weight below the 10th percentile for gestational age (GA) *(Grivell et al., 2012)*.

Intrauterine growth restriction is one of the most significant causes of perinatal morbidity and mortality *(Marconi et al., 2010)*. There are no proven preventive or therapeutic strategies. Researches have focused on the identification of IUGR and prediction of outcome to optimize the timing of delivery *(Juriy and Eik-Nes, 2010)*.

The TCD is a very good indicator of GA in the second trimester, and it is the best dater of pregnancy in the third trimester because it is rarely affected by aberrations in fetal growth. TCD has a curvilinear relation with GA and is not much affected by the shape of the head or by growth disturbances. Its mid-pregnancy maximum transverse diameter in millimeters reflects GA in weeks. TCD monogram is reliable and accurate in predicting GA even at extremes of fetal growth *(Goel et al., 2010)*.

This parameter is the most sensitive in predicting nutritional problems of the fetus, being influenced by the thickness of the abdominal wall and by the amount of the hepatic glycogen stores. It is used for estimation of fetal weight. When the AC measurement falls below the 2.5th percentile for GA, IUGR may be suspected *(Reece and Hagay, 2010)*.

The aim of the present study was to compare TCD/AC ratio in both normal and growth restricted fetuses in second and third trimesters and to find any correlation between TCD/AC ratio and EFW.

PATIENTS AND METHODS

The study was carried out on 100 pregnant females attending the outpatient clinic of El-Sayed Galal University Hospital and Damanhour Teaching Hospital in the period between March 2019 till May 2020 and the patients were divided into two main equal groups: Group I included pregnant females with normally growing fetuses and Group II included pregnant females with growth restricted fetuses above 20 weeks of gestation.

Inclusion criteria: Singleton pregnancy, GA above 20 weeks of gestation and known accurate GA (sure of last menstrual period or having 1st trimester scan).

Exclusion criteria: Congenital fetal anomalies, any conditions that can affect fetal biometric measurements (except IUGR).

All cases included in the study were submitted to the following:

A. **Full history taking (medical and obstetrical):** Age, gravidity, parity and date of last normal menstrual period to estimate the GA.

B. **Complete general examination:** Vital signs, head & neck, chest and extremities examination.

C. **Obstetrical examination:** Fundal level and obstetric grips.

D. **Routine antenatal laboratory investigations.**

E. **Detailed ultrasound scanning trans-abdominally (GE-e6) (2Mhz to 8Mhz) to assess:** GA, exclude multiple pregnancies, exclude fetal congenital anomalies, fetal biometry including: BPD, HC, TCD, AC and FL, EFW, AFI and calculation of TCD/AC ratio × 100 for each case in both groups.

F. **Functional assessment of the fetal condition using:** BPP and Doppler study of UA and MCA if needed.

Measurements to confirm GA and to diagnose IUGR:

BPD and HC are both obtained from the trans-thalamic view and all measured data calculating the GA according to Hadlock tables *(Loughna et al., 2010).* The TCD was calculated using the trans-cerebellar view, measuring the maximum transverse diameter of the dumbbell shaped structure in the posterior cranial fossa (cerebellum) (the measuring data calculating the GA according to Goldstein table) *(Baschat et al., 2010).* The AC and FL were measured. The measuring data calculating the GA was according to Headlock table *(Loughna et al., 2010).* Assessment of the amniotic fluid volume was by using the AFI.

Doppler studies:

Doppler studies of the UA were sampled by color Doppler ultrasound and pulsed waves Doppler, all Doppler examination were performed using (GE-e6) (2Mhz to 8Mhz).

Statistical analysis:

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). P-value <0.05 was considered significant; t-test was used to compare the parametric data while, Mann Whitney test was used to compare the nonparametric data and person coefficient was used.

RESULTS

The mean age of patients in group (1 control group) was 26.65±4.433 years; age ranged between 18 – 38 years, while the mean age in the group (2 IUGR group) was 28.23±4.806 years, and age ranged between 18 – 39 years and there was no statistically significant difference between the two studied groups (P = 0.091) **(Table 1)**.

Table (1): Maternal age in both groups (normal and IUGR)

Age (years) \ Groups	Group 1 (N=50) (control group)	Group 2 (N=50) IUGR	P Value
Mean	26.65	28.23	
S.D.	4.433	4.806	
Min	18	18	0.091
Max	38	39	
Range	18 – 38	18 – 39	

The mean TCD/AC × 100 of patients in group (1 control group) was 13.436±1.0396; TCD/AC ranged between (10.08 – 16.16), while the mean in group (2 the IUGR group) was 15.998±0.9497, TCD/AC ranged between (14.2 -18.3) and there was statistically significant difference between the two studied groups (p < 0.001) **(Table 2)**.

Table (2): Percent of TCD/AC in both groups (normal and IUGR)

TCD/AC ×100 \ Groups	Group 1 (N=50)	Group 2 (N=50)	P Value
Mean	13.436	15.998	
S.D.	1.0396	0.9497	
Min	10.08	14.2	<0.001
Max	16.16	18.3	
Range	10.08– 16.16	14.2– 18.3	

The diagnostic accuracy of TCD/AC was evaluated for the overall series using receiver operating characteristic (ROC) curve analysis. The ROC curve analysis suggested that the most useful cutoff value of TCD/AC × 100 was 13.75%, where the sum of sensitivity (100.0%) and specificity (63.33%) was the highest **(Table 3** and **Fig. 1)**.
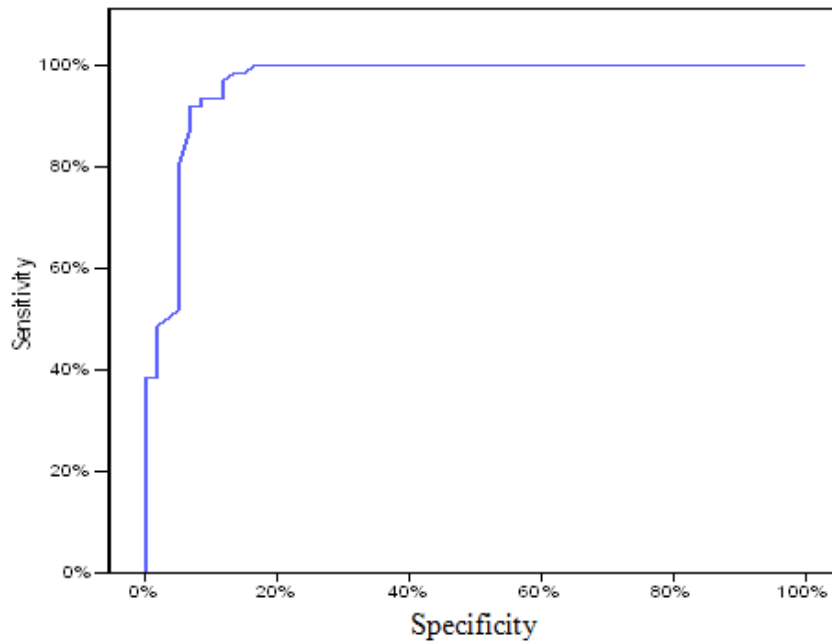
Figure (1):   ROC curve for TCD/AC

Table (3): Sensitivity, specificity and accuracy for TCD/AC ratio in diagnosis of IUGR

Parameters / IUGR		Control	Cases	Sensitivity	Specificity	PPV	NPV	Accuracy
TCD/AC	<13.75	32	0	100.0	63.33	73.17	100.0	81.67
	≥13.75	18	50					

The mean EFW Using AC, BPD, FL of patients in group (1 control group) was 2177.717 ±806.131g; EFW Using AC, BPD, FL ranged between (989 – 3895g), while the mean EFW Using AC, BPD, FL in the group (2 IUGR group) was 1758.483±596.924g, EFW Using AC, BPD, FL ranged between (527 – 2992g) and by using Mann Whitney test there was a statistically significant difference between the two studied groups (p=0.003) **(Table 4)**.

Table (4): EFW Using AC, BPD, and FL in both groups (normal and IUGR)

Using AC, BPD, FL	Group 1 (N=50)	Group 2 (N=50)	P Value
Median	2100.0	1750.0	
Mean(gm)	2177.717	1758.483	
S.D.	806.131	596.924	U=24.3
Min	989	527	0.003
Max	3895	2992	
Range	989 – 3895	527 – 2992	

Mann Whitneyutest

The mean TCD/AC 100 of patients in group (1 control group) was 13.44±1.04; ranged between (10.08 – 16.16) while the mean EFW was 2223.53±882.56g, ranged between (754 – 4127g). There was no statistically significant relation between the TCD/AC ×100 and EFW of patients P = 0.113. The mean TCD/AC in the group (2 IUGR group) was 16±0.95, TCD/AC ranged between (14.20 – 18.30), while the mean EFW was 1476.60±598.50g, ranged between (523.0 – 2687.0g) and there was no statistically significant relation where P = 0.806 **(Table 5)**.

Table (5): Correlation between TCD/AC ratio and EFW in both groups

Correlation Groups	TCD/AC	EFW	r	P
Group 1				
Mean (g)	13.44	2223.53		
S.D.	1.04	882.56		
Min	10.08	754.0	0.207	0.113
Max	16.16	4127.0		
Range	10.08 - 16.16	754.0 – 4127.0		
Group 2				
Mean (g)	16.0	1476.60		
S.D.	0.95	598.50		
Min	14.20	523.0	0.032	0.806
Max	18.30	2687.0		
Range	14.20 – 18.30	523.0 – 2687.0		

r: Pearson coefficient

The mean UA (S/D) of patients in group (1 control group) was 2.7087±0.75692; ranged between 1.79 – 5.7, while the mean UA (S/D) in the group (2 IUGR group) was 3.417±1.5165, ranged between (1.85 – 8.3) and there was statistically significant difference between the two studied groups (P = 0.006).

The mean UA (RI) of patients in group (1 control group) was 0.6558±0.1251; (RI) ranged between 0.4 – 1.03, while the mean UA (RI) in the group (2 IUGR group) was 0.6751±0.1543, ranged between 0.2 – 1.1 and there was no statistically significant difference between the two studied groups (P = 0.494).

The mean UA (PI) of patients in group (1 control group) was 0.8922±0.2171; ranged between 0.1 – 1.82, while the mean UA (PI) in the group (2 IUGR group) was1.1405±0.4497, ranged between 0.7– 2.3 and there was a statistically significant difference between the two studied groups (P = 0.042) **(Table 6)**.

Table (6): UA Doppler indices in both groups (normal and IUGR)

Indices \ Groups	Group 1	Group 2	P Value
S/D	**Control**	**IUGR**	
Mean	2.7087	3.417	
S.D.	0.75692	1.5165	
Min	1.79	1.85	0.006
Max	5.7	8.3	
Range	1.79 – 5.7	1.85– 8.3	
RI			
Mean	0.6558	0.6751	
S.D.	0.1251	0.1543	
Min	0.4	0.2	0.494
Max	1.03	1.1	
Range	0.4– 1.03	0.2 – 1.1	
PI			
Mean	0.8922	1.1405	
S.D.	0.2171	0.4497	
Min	0.1	0.7	0.042
Max	1.82	2.3	
Range	0.1– 1.82	0.7– 2.3	

DISCUSSION

This study showed that, cerebellar diameter was even less affected than the HC suggesting a preferential mechanism in the preservation of cerebellar growth relative to other cranial structures. These results were consistent with data from studies in primate models which demonstrate that, even within the brain, blood flow to the cerebellum, brain stem and midbrain was higher than that of cerebrum *(Sifianou, 2010)*. The blood flow shifts mainly to the central parts including brain, heart and adrenal glands, in chronic asphyxia, cerebellar blood flow remains unchanged as a consequence of redistribution of cardiac output. The TCD is the least affected biometric parameter so; TCD/AC could be a sensitive method of detecting IUGR at any GA *(Scifres et al., 2010)*.

Dhumale et al. (2010) found that asymmetrically growth impaired fetuses had a TCD lower than expected put within the normal range suggesting this measurement is useful for estimating GA in these cases.

Khan et al. (2013) found that TCD/AC ratio is strongly associated with IUGR. TCD could readily be measured after 11 weeks and it has a linear correlation with GA unlike BPD and TCD is not affected by abnormal shape of the skull. It is a better predictor of GA than BPD and seems to be minimally affected in abnormal fetal growth.

As TCD is the least affected biometric parameter, AC is the most affected parameter; TCD/AC could be a sensitive method of detecting asymmetrical IUGR at any GA *(Wright et al., 2020)*. The findings from this study help identification and assessment of the fetuses and create possibility for early intervention and therapy to prevent fetal morbidity and mortality. The normal fetal

TCD demonstrates a more than twofold increase in size during the second half of pregnancy. Type of IUGR may have an influence on cerebellar growth. It is believed that the cerebellum of the fetus with symmetrical IUGR may be affected to some degree *(Srikumar et al., 2017).*

Sharma et al. (2014) found that the sensitivity of TCD/AC ratio in predicting IUGR was as high as 98% in asymmetrical IUGR, whereas it was only 71% in symmetrical IUGR.

Olsen et al. (2010) showed that in 88 from 122, cortical blood flow was decreased in asphyxiated fetuses, but cerebellar blood flow remained unchanged. *Bhimarao et al. (2015)* found 80% of values for the IUGR fetuses to be above the upper limit of the normal range. Raised TCD/AC measurements suggested the presence of fetal growth restriction; it was pointed out by *Rashid et al. (2018)* that severe growth restriction (birth weight below the third percentile) may be associated with normal TCD/AC values. The same authors put forward that this could be due to either a reduced cerebellar growth in severe growth restriction or the presence of a genetically small fetus and therefore a small cerebellum.

The results of this study demonstrated the usefulness of the single cut-off value of the TCD/AC ratio which may contribute to the early identification of SGA infants. The best cut-off value of TCD/AC ratio for predicting IUGR was 13.75%, giving the sensitivity, specificity, positive predictive value and negative predictive value of 100%, 63.33%, 73.17% and 100%, respectively as shown in Table 14. The TCD/AC ratio in this study was found to have a rather high sensitivity 100% and specificity 63.33%, when the ratio above this value we can diagnose IUGR.

Uikey et al. (2016) found that the TCD/AC ratio has as higher sensitivity as 100%. The specificity in this study was 80.25%, indicating a high chance of a negative test among non-IUGR fetuses or a lower chance of premature termination of non-IUGR fetuses.

However, *Twomey et al. (2016)* found that, 86 infants with IUGR from176 with cut-off value of TCD/AC, was 15.4%, giving the sensitivity, specificity, positive predictive value and negative predictive value of 73.26%, 80.25%, 79.75% and 73.86%, respectively.

The difference between the TCD/AC ratios from our results and those from other studies could probably due to different population types, necessitating the use of monograms specific to Egyptian population *(Wright et al., 2020).*

The TCD/AC ratio, which utilizes a single cut-off value independent of GA, could improve diagnostic sensitivity and specificity in IUGR cases. The possible contribution of the TCD/AC ratio in identifying the fetal growth failure itself, which is very important to be further evaluated.

In our study there was no correlation between TCD/AC ratio and EFW however; *Dhumale et al. (2010)* found that, the TCD/AC ratio was abnormal in 80% of the IUGR infants.

In our study, there was no statistical significant correlation between TCD/AC ratio and UA Doppler or MCA, and there was no studies signify the relation between them. There was a statistical

significant correlation between TCD/AC ratio and perinatal mortality. In control group, the perinatal mortality was 0.06 %, while was 0.12 % in IUGR group, the perinatal mortality rate in IUGR group was approximately two fold increase than normal.

Chawanpaiboon and coworkers (2010) demonstrated that the subset of SGA fetuses with elevated TCD/AC ratio displayed a relatively poor outcome. In contrast, *Meyer et al. (2012)* found no difference in perinatal mortality or birth weight between the subset of fetuses with a normal or raised TCD/AC relationship.

CONCLUSION

1. In IUGR fetuses, the fetal TCD was less affected than fetal HC suggesting preferential preservation of cerebellar growth relative to other cranial structures.

2. The TCD/AC ratio was helpful in recognizing abnormal fetal growth. Even when the GA was uncertain since this ratio was gestational age-independent.

3. A TCD/AC ratio above the 13.75% was suspicious of growth restriction and therefore an indication for further investigations, such as fetal and placental velocimetry by Doppler ultrasound.

4. In IUGR, use of UA Doppler velocimetry was important, together with other tests of fetal well-being, may provide a rationale for timing screening for IUGR.

5. There was no statistical significant correlation between TCD/AC ratio and expected fetal weight in IUGR in spite of significant difference in EFW between IUGR and normal population.

6. There was no statistical significant correlation between TCD/AC ratio and Doppler indices of either UA or MCA in spite of the hemodynamic rearrangement of blood flow to brain in cases of IUGR.

RECOMMENDATIONS

• Trans-cerebellar diameter should be used routinely in all obstetric ultrasound evaluation as an indicator for GA, especially in late pregnancy with unknown menstrual GA.

• Use of routine measure for TCD/AC percent may give earlier and better diagnosis of IUGR. Again, it can indicate more and intensive monitoring of those cases with abnormal TCD/AC ratio.

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إستخدام الموجات الفوق صوتية فى قياس النسبة بين عرض المخيخ ومحيط بطن الجنين فى الحالات الطبيعية وحالات نقص نمو الجنين خلال الثلاثة أشهر الثانية والثالثة من الحمل

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خلفيــة البحــث: نقـص نمـو الجنـين داخـل الـرحم غالبـا مـا يصـاحبه زيـادة فـى معـدل الوفيـات حيـث أن الـدم المتـدفق إلـى المشيمة فـى نقـص نمـو الجنـين داخـل الـرحم غالبـا مـا يتـأثر, ممـا يـؤدى الـى ضـعف الـدورة الدمويـة داخـل المشيمة و قد يتسبب فى نقص نمو الجنين داخل الرحم.

الهـدف مـن البحـث: مقارنـة النسـبة بـين عـرض المخـيخ ومحـيط بطـن الجنـين فـى الحـالات الطبيعيـة وحـالات مـرض نقـص نمـو الجنـين داخـل الرحم ما بعد الاسبوع العشرين من الحمل.

المريضـات وطـرق البحـث: أجريـت هـذه الدراسـة بمستشـفي سـيد جـلال الجـامعي ومستشـفي دمنهـور التعليمـي فـي الفتـرة بـين مـارس 2019 ومـايو 2020 و قـد اجريـت الدراسـة علـى 100 مـن السـيدات الحوامـل فـى جنـين واحـد وتـم تقسـيمهم لمجمـوعتين رئيسـيتين: **المجموعـة الأولـى:** تتضـمن 50 حالـة مـن الحـالات الطبيعيـة مـا بعـد الاسبوع العشـرين مـن الحمـل. **المجموعـة الثانيـة:** تتضـمن 50 حالـة مـن حـالات نقـص نمـو الجنـين مـا بعد الاسبوع العشرين من الحمل.

نتـائج البحـث: قيـاس النسـبة بـين عـرض المخـيخ و محـيط بطـن الجنـين وذلـك مـا بعـد الاسـبوع العشـرين مـن الحمـل قـد يسـاعد علـى سـرعة الاكتشاف المبكر لحالات نقص نمو الجنين داخل الرحم.

الإستنتاج: في الأجنة المتخلفة عن النمو داخل الرحم، يكون قطر الجنين عبر المخيخ أقل تأثراً من محيط رأس الجنين مما يوحي بالحفظ التفضيلي لنمو المخيخ نسبة إلى الهياكل القحفية الأخرى وقطر محيط المخيخ/ نسبة محيط البطن مفيد في التعرف على نمو الجنين غير الطبيعي حتى عندما يكون عمر الحمل غير مؤكد لأن هذه النسبة مستقلة عن عمر الحمل.

الكلمات الدالة: الموجات فوق الصوتية، عرض المخيخ، محيط بطن الجنين.