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Original Article

Radiology Section

Predictive Accuracy of Foetal Trascerebellar Diameter in Gestational Age Estimation with Foetal Cerebellar Grading

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ABSTRACT

Introduction: Determination of gestational age is important in obstetrics for management of pregnancy and evaluation of foetal development. An error in the gestational age estimation results in prematurity and post maturity and, if expected date of delivery is not known, higher perinatal mortality is the obvious outcome.

Aim: To evaluate accuracy of transcerebellar diameter in gestational age estimation, to determine the ratio between transcerebellar diameter and abdominal circumference as a gestational age independent parameter, and to study the change in ultrasonographic appearance of the foetal cerebellum with advancing gestation and its grading.

Materials and Methods: In 100 normal singleton pregnant women between 15 to 37 weeks of gestation, Biparietal Diameter (BPD), Head Circumference (HC), Abdominal circumference (AC) and Femur Length (FL) and Transcerebellar Diameter (TCD) were measured for assessing the sonological gestational age. TCD/AC ratio was also calculated and simultaneously, the ultrasonographic appearance of the foetal cerebella with advancing gestation were noted and grouped into three grades.

Results: In the present study, statistically significant linear relationship between TCD and gestational age in normal pregnancies was noted. TCD measured in millimeters was almost equal to gestational age up to 23 weeks. The TCD/AC ratio remained fairly constant throughout gestational age with a mean ± SD of 13.76 ± 0.77. As with advancing gestation, foetal cerebellum showed a gradual change in US appearance of the progressing from Grade I to Grade III.

Conclusion: Correlation and regression analysis indicated a good correlation of TCD with gestational age and other. Hence, TCD can be used as a single growth parameter to predict the gestational age in cases where LMP (Last Menstrual Period) is uncertain. TCD/AC ratio can be used as a good tool to diagnose asymmetric Intra Uterine Growth Retardation (IUGR) in those with ratio exceeding 2 SDs as it is gestational age independent factor which remained fairly constant throughout gestation. We observed a gradual and progressive change in ultrasound appearance of foetal cerebellum from Grade 1 to Grade 3 with advancing gestation.

Keywords: Biparietal diameter, Cerebellum, Foetal biometry, Ultrasound

INTRODUCTION

Determination of gestational age is important in obstetrics for management of pregnancy and evaluation of foetal development. An error in the gestational age estimation results in prematurity and post maturity and, if expected date of delivery is not known, higher perinatal mortality is the obvious outcome. Several clinical criterias are utilized to assess gestational age, among which last menstrual period preceded by normal cycle shows best correlation. However, it becomes less reliable when last menstrual period is not certain. Presently, the most effective way to date pregnancy is by the use of ultrasound [1,2].

Several sonographically derived foetal biometric parameters used to date pregnancy include BPD, HC, AC and FL [3,4].But with these parameters, there is increasing variability in assessing gestational age as the pregnancy advances [5-7]. TCD, a measurement in the posterior fossa of the foetal brain is least affected by external factors and foetal growth abnormalities which allows its use for gestational age determination. TCD measurement can be used as a new parameter to estimate the gestational age of foetus in both normal and intrauterine growth retarded pregnancies [8].

Human foetal cerebellum changes its appearance with advancing gestation. These gradual changes can be

appreciated on ultrasound which include changes in both shape and echogenicity with advancing gestation. These changes may be a reflection of the histologic development of the foetal cerebellum during pregnancy [9]. These changes can be graded and thus grading system assessment not only helps in assessing development of the foetus but also structural anomalies affecting posterior fossa can be detected.

The present study was undertaken to evaluate the usefulness of TCD as against other conventional parameters in normal pregnancies. TCD/AC ratio was also assessed with an idea of its use as a potential parameter for foetal growth abnormalities.

MATERIALS AND METHODS

This exploratory study was conducted for over a period of one year from December 2013 to November 2014 in Department of Radiodiagnosis, Mysore Medical College, Mysuru, India. Informed consent was taken and ethical clearance was issued. The study included 100 pregnant women of singleton pregnancy undergoing obstetric ultrasound between 15- 37 weeks and confirmed gestational age (regular menstrual history with known last menstrual period and/or ultrasound confirmation of gestational age by means of crown rump length measurement). Multiple gestation, anomalous pregnancies, hypertension, diabetes mellitus, cardiac diseases, and failure to clearly visualize/measure the foetal cerebellum were excluded from the study. Ultrasonography of all selected cases was performed on ESAOTE MyLab 40 ultrasound machine with a 3.5 MHz convex array transducer. Patients were explained about the procedure and it was performed in supine position with hips and knees in extension. The transducer was placed on the skin surface after applying the coupling agent.

In each patient TCD, BPD, HC, FL, and AC were recorded. TCD was measured by identifying the cerebellum in the posterior fossa and measuring it in from outer to outer extent [Table/Fig-1].The thalamic plane used for BPD [Table/Fig-2] was then obtained, the transducer was then rotated about 30 degrees below the thalamic plane to see the cerebellum as described by Goldstein. The abdominal circumference [Table/Fig-3] was obtained from a transaxial view at the level of the junction of umbilical vein and left portal vein. TCD/AC ratio was calculated by dividing the TCD by the AC and then multiplying by 100. Simultaneously, the US appearance of the foetal cerebella was noted and grouped into three grades as described by Hashimoto K et al., [9]. Grade I shows cerebellum as hypoechoic, “eyeglass” shape, Grade II as intermediate echogenicity with “dumbbell” outline, and Grade III as hyperechoic, “fan” shape. These grades were analyzed in relation to GA and TCD. The median GA and TCD were calculated for Grade I, Grade II, and Grade III respectively.

STATISTICAL ANALYSIS

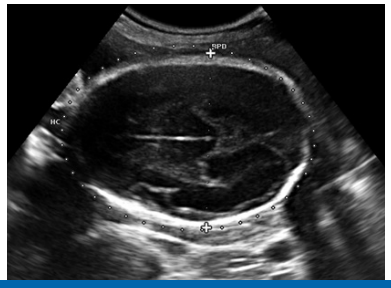
Regression analysis was done to compare each ultrasonographically measured parameters i.e., TCD, BPD, HC, AC and FL with the gestational age of foetus. Correlation coefficients were then used to compare TCD with BPD, HC, AC and FL in normal pregnancies. All the statistical calculations were done through SPSS for windows (version 20.0).

RESULTS

Analysis of 100 normal singleton pregnancies showed a statistically significant linear relationship between TCD and gestational age (R^2-0.98; $p<0.0001$). Regression analysis showed that, out of all parameters TCD shows best correlation with gestational age [Table/Fig-4]. Scatter diagram was plotted showing correlation between GA and TCD [Table/Fig-5]. Good correlation was found between TCD and other parameters [Table/Fig-6]. By using the ultrasonographically derived data nomogram [Table/Fig-7] was devised for TCD. The nomogram shows mean measurements in millimeter (mm) for TCD at 5th, 50th and 95th percentile for the corresponding gestational age.

TCD/AC Ratio

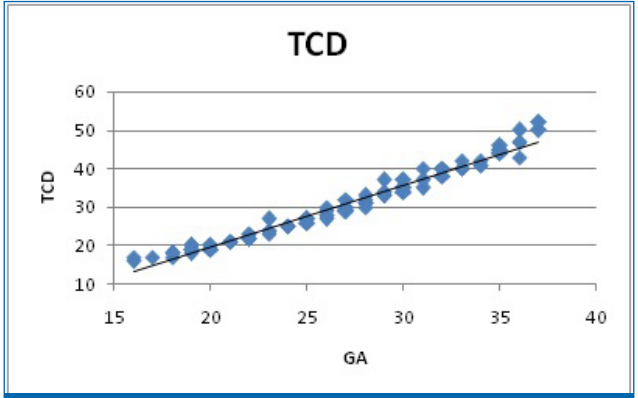
Several studies have indicated that TCD/AC ratio 2SD above the mean is a sensitive predictor of IUGR. Mean TCD/AC ratio was found to be 13.76±0.77 (SD) (mean+2SD=15.32) which remained fairly constant throughout pregnancy and thus it is a useful gestational age independent parameter. In present study 1 out of 2 foetuses with TCD/AC ratio more than 2SDs showed asymmetric IUGR on neonatal examination, while in



[Table/Fig-1]: Transaxial view showing appearance and measurement of transcerebellar diameter. **[Table/Fig-2]:** Transaxial view showing calipers indicating measurement of BPD and HC. **[Table/Fig-3]:** Transaxial view showing calipers indicating measurement of AC.

Parameters Compared	R^2	p-value
GA Vs BPD	0.974	0.0001
GA Vs HC	0.975	0.0001
GA Vs AC	0.986	0.0001
GA Vs FL	0.985	0.0001
GA Vs TCD	0.986	0.0001

[Table/Fig-4]: Table showing correlation of GA with BPD, HC, AC, FL and TCD.



[Table/Fig-5]: Scatter diagram showing correlation between GA and TCD.

Parameters Compared	R^2	p-value
TCD Vs BPD	0.96	0.0001
TCD Vs HC	0.95	0.0001
TCD Vs AC	0.98	0.0001
TCD Vs FL	0.97	0.0001

[Table/Fig-6]: Table showing correlation of TCD with BPD, HC, AC, and FL.

other case neonatal follow-up could not be done.

Foetal Cerebellar Grading

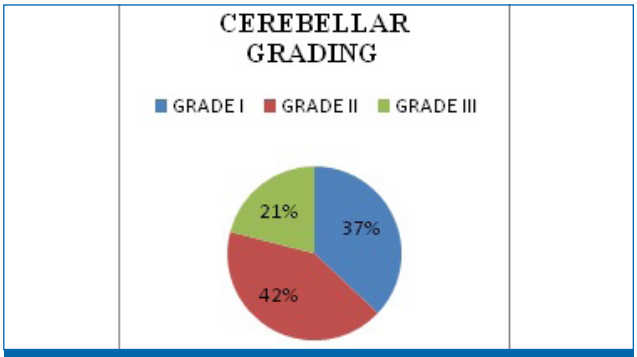
In this study, the change in the US appearance of the foetal cerebellum with advancing gestation was noted and grouped into grades as described by Hashimoto K et al., [9]. These grades were analyzed in relation to GA and TCD. Cerebella in 37 (37%), 42 (42%), and 21 (21%) of 100 subjects [Table/Fig-8] were classified as Grade I (hypoechoic, "eyeglass" shape), Grade II (intermediate echogenicity, "dumbbell" outline), and Grade III (hyperechoic, "fan" shape), respectively.

With advancing gestation, the dominant Grade changed from I to III gradually and progressively. The median GA and TCD, respectively, were 20 weeks and 20 mm for Grade I [Table/Fig-9], 28 weeks and 32 mm for Grade II [Table/Fig-10], and 35 weeks and 44 mm for Grade III [Table/Fig-11].

All 33 cases before 24 weeks showed Grade I cerebellum, and all 16 cases after 33 weeks showed Grade III [Table/Fig-12]. Between 24 and 33 weeks, 4 (7.8%), 42 (82.3%), and 5 (9.8%) of 51 cases were Grades I, II, and III, respectively. The

GA	5th Percentile	50th Percentile	95th Percentile
16th week	16.0	16.5	17.0
17th week	17.0	17.0	17.0
18th week	17.0	18.0	18.0
19th week	19.0	19.0	20.0
20th week	19.0	19.0	20.0
21st week	21.0	21.0	21.0
22nd week	22.0	22.0	23.0
23rd week	23.0	23.5	27.0
24th week	24.0	25.0	25.0
25th week	26.0	27.0	27.0
26th week	27.0	28.0	30.0
27th week	29.0	29.0	32.0
28th week	30.0	31.0	33.0
29th week	33.0	34.0	36.0
30th week	34.0	34.0	37.0
31st week	35.0	37.0	40.0
32nd week	38.0	39.0	40.0
33rd week	40.0	40.0	42.0
34th week	41.0	42.0	42.0
35th week	44.0	44.0	46.0
36th week	43.0	47.0	50.0
37th week	50.0	50.0	52.0

[Table/Fig-7]: Normogram showing mean TCD (mm) measurements at 5th, 50th and 95th percentile for the corresponding gestational age.

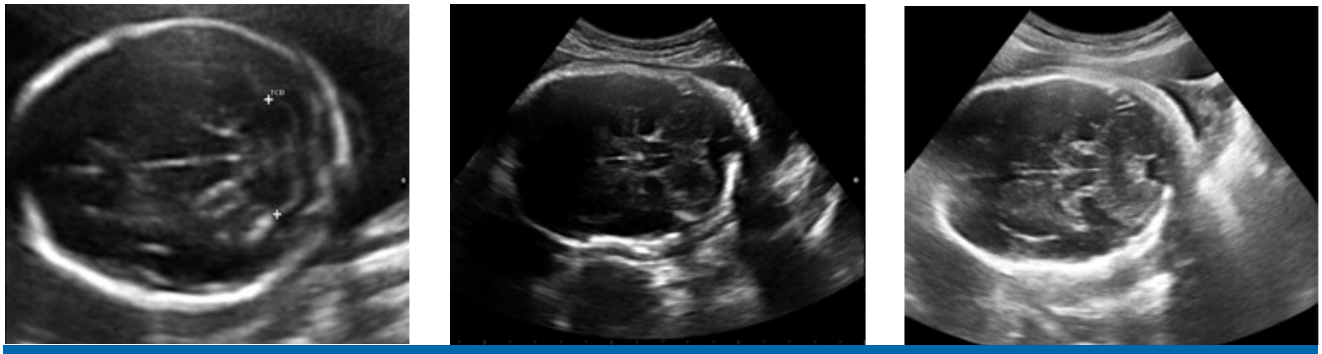


[Table/Fig-8]: Pie diagram representing percentage of cerebellar grades in the study group.

Grade II cerebellum was distributed over a 10-week period. Similarly, when TCD was 24 mm or less or 41 mm or greater, all the cases were Grade I and III, respectively. Between 25 and 40 mm, 4 (7.8%), 42 (82.3%), and 5 (9.8%) of 51 cases were Grades I, II, and III, respectively.

DISCUSSION

Objective knowledge of the expected date of delivery is critically important for pregnancy management from the first trimester to delivery and also it influences the method of delivery, elective



[Table/Fig-9]: Grade I cerebellum. Transcerebellar US view at 21 weeks gestation. Cerebellar hemispheres are cystic and show "a pair of eyeglasses" appearance . **[Table/Fig-10]:** Grade II cerebellum.Transcerebellar US view at 31 weeks gestation. Cerebellar hemispheres are oval and echogenic with "dumbbell-like" outline and the vermis has developed. **[Table/Fig-11]:** TGrade III cerebellum. Transcerebellar US view at 35 weeks gestation. Cerebellar hemispheres show "fan" shape and the whole cerebellum is homogeneously echogenic.

GA(weeks)	Number of Cases	Grade I	Grade II	Grade III
15- 23	33	33	0	0
24-33	51	4	42	5
34-38	16	0	0	16
Total	100	37	42	21

[Table/Fig-12]: Table showing gradation of cerebellum.

planned induction of labor and elective caesarean for previous caesarean section deliveries and management of high risk pregnancies. In patients whose expected date of delivery is not known as compared to those in whom it is known, a higher incidence of perinatal mortality has been reported [1]. LMP preceded by normal cycle is known to best correlate with the gestational age when compared to the various clinical criteria available, but it is not reliable when a woman is uncertain about her last menstrual period. The biometric parameters used for gestational age assessment are BPD, HC, AC and FL [2-4]. However, each of these parameters has their own limitation. The variability in predicting gestational age with these parameters goes on increasing because of the biologic variability that occurs with advancing gestational age [5,6]. TCD has shown high consistency in predicting GA in both singleton and twin gestations [10]. TCD represents an independent biometric parameter as shown in this study. The foetal cerebellum can be visualized as early as 10-20 postmenstrual weeks. It grows in a linear pattern in the second trimester but the curve flattens in third trimester [11].

Anatomically, the cerebellum is situated in posterior fossa where the dense petrous ridges surround it laterally and occipital bone inferiorly, which is aligned perpendicular to the plane of maximum extrinsic compression. Hence, it appears to be able to withstand deformation by extrinsic pressure better than the parietal bones. The maximum measurement of this organ is its transverse dimension and its size correlates well with GA. Due to this, TCD can be used where it is difficult to measure BPD or in cases where there are variations in size and shape of head [12].

In this study, it was noted that early sonographic visualization of cerebellum occurred as early as 15 to 16 weeks of gestation. The characteristic appearance of cerebellum on ultrasound is seen as two lobules on either side of midline in the posterior cranial fossa.There is a good correlation between BPD and TCD (R^2 = 0.96, p-value = 0.001) similar to the study done by Mcleary RD et al., [13] and Naseem F et al., [14]. In case of breech presentation, extrinsic pressure may deform the skull and decrease the biparietal diameter, however TCD remains relatively unaffected and Mcleary RD et al., [13] have proposed that TCD remains more reliable method of gestational age estimation, particularly in breech presentation. In the present study, TCD showed linear relationship with gestational age (R2 = 0.986, p-value = 0.001) similar to the study done by Goldstein I et al., [15] and Bansal M et al., [16]. TCD nomogram was established from ultrasonographically measured data which can be used for estimating the gestational age of foetus.

In the present Study, measurement of TCD in millimeters up to 23 weeks is equal to gestational age as similar to study done by Reece EA et al., [17] in which they found that TCD from 15th to 24th week of gestation in millimeters is equivalent to the gestation age in weeks. However, after 24 weeks the TCD in millimeters exceeds gestational age in weeks.

In this study, the relationship of transverse cerebellar diameter to gestational age was considered in normal foetuses only. However, TCD/AC ratio was assessed with an idea of its use as a potential parameter for foetal growth abnormalities. Two separate studies done by Dhumale H et al., [18] and Malik R et al., [19] found the TCD/AC ratio was fairly constant throughout gestation and found it to be a good tool to diagnose asymmetric IUGR in those with ratio exceeding 2SDs. Our study showed similar findings of TCD/AC ratio which was fairly constant with a mean of 13.76 and SD of 0.77 [Table/Fig-13]. In the present study, 1 out of 2 foetuses with TCD/AC

ratio more than 2SDs was shown to have asymmeteric IUGR on neonatal examination, while in other case neonatal follow up could not be done. Behrman RE et al., [20] in their study on primate models demonstrated that cerebellar blood flow is relatively spared in cases of IUGR which could explain above observation. However, the AC is acutely affected in IUGR and the reason for this is depletion of foetal hepatic glycogen and subcutaneous fat stores in early stages of IUGR which is reflected as decrease in foetal abdominal circumference.This makes foetal AC to be an earliest parameter and sensitive predictor of assymetrical IUGR [21]. An important observation noted in two separate studies by Lee W et al., [22] and Campbell WA et al., [23] that the TCD/AC ratio may not be sensitive to diagnose symmetrical IUGR where both TCD and AC may be equally affected. The other morphometric ratio used in detection of IUGR is FL/AC ratio, but this ratio is less sensitive because there is substantial overlap of FL/AC ratio in normal and growth restricted foetuses without a single cut off value to identify IUGR. Another study by Bhimarao et al., [24] also indicated that TCD/AC ratio is gestational age independent which has a better diagnostic validity and accuracy compared to HC/AC ratio in predicting asymmetric IUGR.

Two studies done by Tongsonng T et al., [25] and Campbell et al., [23] studied the usefulness of TCD/AC ratio in IUGR foetuses, concluded that the TCD/AC ratio cut off value suggestive of IUGR was 15.4 and 15.9. The comparison of present study results [Table/Fig-13] with the above mentioned studies showed that the TCD/AC ratio is a gestational age independent constant parameter and also the mean TCD/AC ratio for normal foetal growth and the 2SD or cut off values for diagnosis of IUGR are similar between the present study (15.32) and their studies.

Similar to study done by Hashimoto et al., [9] in which they classified and graded the ultrasonographic appearance of foetal cerebellum, with advancing gestation, the dominant Grade changed from I to III gradually and progressively. We observed that Grade II cerebellum was distributed over a 10-week period. The Grade II cerebellum represents a transitional stage in development and the timing of these ultrasound changes among each individual perhaps be difference for months, which reflects the rate of anatomic development [11].

Clinical implication: Incorporating the results of TCD with combination of other foetal biometric parameters further improves accurate gestational dating. TCD/AC ratio is gestational age independent parameter. Thus, helps in detecting IUGR in women with unknown dates particularly in third trimester. Serial monitoring of cerebellar growth with grading system allows to understand if any deviation from normal growth and development.

Authors	Gestational age (weeks)	Mean and ratio cut off
Dhumale H et al., [18]	18 – 34	13.56±1.21
Malik R et al., [19]	16-40	14.06±0.059
Campbell et al., [23]	15-38	>15.9 (cut off)
Tongsong T et al., [25]	>28	>15.4 (cut off)
Present study	15-38	13.76±0.77

[Table/Fig-13]: Comparison of mean and cut off TCD/AC ratio with other studies.

LIMITATION

As ultrasound is operator dependant, precise measurements of the parameters were relied upon single operator, however since all the measurements were taken by single operator which contributed to decreasing inter operator variability. Adequate visualization of foetal cerebellum in third trimester was limited because of dense shadowing in posterior fossa appeared to be another technical limitation.

CONCLUSION

TCD shows a good correlation with gestation age and also with other biometric parameters for assessing gestational age in normal pregnancies at 15 to 37 weeks of gestation. TCD/AC ratio can be used as good parameter to assess and diagnose asymmetric IUGR in those with ratio exceeding 2SDs as it remains fairly constant throughout gestation.

A gradual change in US appearance of the foetal cerebellum is seen with advancing gestation and with the help of the grading system it may be useful to understand the normal development of the human cerebellum and to evaluate abnormal growth and maturation in normal and complicated pregnancies.

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