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Assessment of Transcerebellar Diameter and Femur Length of the Foetus by Ultrasound for the Determination of Gestational Age in the Third Trimester of Pregnancy

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Abstract

Introduction: *Gestational age estimation is of prime importance in anticipating the day of delivery and preventing obstetric complications. Several ultrasonogram measured foetal parameters arc used to determine gestational age which include crown -rump length (CRL), biparietal diameter (BPD), head circumference (HC), femur length (FL), abdominal circumference (AC) and trans-cerebellar diameter (TCD). TCD and FL have been proposed as variables which are not subjected to much variation due to intra-uterine forces other than growth of the foetus.*

Materials and Methods: *A hospital-based, prospective study was conducted in the Department of Radiology, Andhra Medical College, Visakhapatnam between October 2018 and February 2020 on 100 normal singleton pregnant women with normal foetal growth pattern.*

Results: *The study showed that the study participants were mostly young women (mean age= 25.6±4.53) with majority in the 21-25 years age group (74%) and primigravida (61%). The gestational age as determined by CRL in first trimester correlated significantly [p<0.001] with the TCD (mm) values (r^2 = 0.9545) and FL (mm) values (r^2 = 0.975) measured in the third trimester. TCD and FL showed significant [p<0.001] positive correlation (r^2 = 0.870) in determining GA. The reliability of the two parameters in assessing gestational age was 87% and a percentage error of 0.082%.*

Conclusion: *The study established the TCD and FL values in third trimester of pregnancy among normal singleton pregnant women. It also showed there was significant correlation of the TCD and FL values measured in third trimester with gestational age determined by CRL in the first trimester. Hence TCD and FL can both be used as reliable and individually used intra-uterine foetal biometric parameters in estimating the gestational age during the third trimester of a normal pregnancy.*

Introduction

Gestational age is not merely a number derived from a mathematical calculation, but, when determined correctly, can save two lives at a time namely the mother and the child. With that prologue in mind, the determination of exact gestational age is of prime importance in anticipating the day of delivery, the anguished pregnancy related complications and monitoring the foetal development during the antenatal

period. Unnecessary emergency caesarean sections, unwanted induction of labour, dysfunctional labour, prematurity, neonatal morbidity and mortality are sequential encounters following an erroneously determined gestational age (GA) or expected date of delivery (EDD).

Several ultrasonogram measured foetal parameters are used to determine gestational age which include the crown -rump length (CRL), biparietal diameter (BPD), head circumference (HC), femur length (FL) and abdominal circumference (AC). CRL is used between 5-10 weeks of gestation and the rest are used between 24-40 weeks of gestation. These parameters have their own variabilities and tend to vary with increasing gestational age and based on the growth of the foetus. The reliability or these parameters in Intra uterine growth retardation, multiple pregnancies, congenital anomalies of the limbs, maternal malnutrition, etc remains questionable[1,2,3,4,5].

Trans-cerebellar diameter (TCD) is a reliable and useful biometric parameter measured by ultrasonogram in estimating gestational age (GA) in the second and third trimester[6].Among the various foetal biometric parameters used to determine gestational age, Trans-cerebellar diameter holds more reliability because of the realistic biological plausibility underneath its usage. The cerebellum is located in a position where it is not liable to change its shape because the dense bony architecture of the petrous and occipital bones helps it to withstand many deforming forces. Thus, any external forces trying to induce change of form or metrics of the brain, like that of the parietal region where the connecting sutures of the cranium are softer in the foetus, shall not have any impact on cerebellum.

The foetal cerebellum can be visualized easily by using ultrasound and therefore imaging the posterior fossa is becoming an integral part of many routine foetal sonograms[7] During the third trimester of pregnancy, TCD varies in a linear fashion while the TCD ratio remains consistent in second and third trimester of pregnancy. Mean TCD as studied at 31 weeks of pregnancy is 34.9 ± 0.885mm[8].

This study shows the usefulness of trans-cerebellar diameter (TCD)as an alternative parameter to determine the foetal gestational age in third trimester by using ultrasound. The study attempted to compare the estimation of foetal gestational age by TCD with that done using Femur length (FL) and verify both with the gestational age calculated based on crown rump length.

Materials and Methods

This is a prospective, hospital-based study conducted in Andhra Medical College, Visakhapatnam between October 2018 and February 2020. The study includes normal singleton pregnant mothers with normal foetal growth pattern attending the Department of Radiology for sonographic evaluation (or as a part of antenatal health check-up) referred from the Department of Obstetrics and Gynaecology, after excluding those ineligible subjects as per exclusion criteria. The sample size is taken assuming a mean TCD of 42.9 mm with standard deviation of 6.3 mm, a sample size of 95 was required to achieve a mean difference of 5 mm with a significance level of 5% and a power of 90%. The study patients encountered during the study period, after meeting the inclusion and exclusion criteria were all included in the study and the final sample size arrived at100.

Inclusion Criteria

1. Normal singleton pregnant mothers with normal foetal growth at 12 - 40 weeks of gestation.

Exclusion Criteria

1. Congenital malformations.
2. Multiple pregnancies.
3. Complicated pregnancies.
4. IUGR.

Results

The study was done on 100 antenatal women attending the Department of Obstetrics and Gynaecology who were evaluated and followed up sonographically in the Department of Radiology, Andhra Medical College, during the study period. The study participants were middle aged women (mean age= 25.6±4.53) with majority in the 21-25 years age group (42%).

Table 1: Age distribution of study population

Age categories (years)	Frequency	Percentage (%)
<20	13	13.0
21-25	42	42.0
26-30	32	32.0
>30	13	13.0
Total	100	100.0

Chi-square for trends: χ^2 value= 25.04, df=3, ***p* value< 0.001**, highly significant

There was a significant difference in the age distribution of the study participants as most of the participants were in the 21-25 years age category (42%) whereas above 30 years age group had lesser representation (13%).

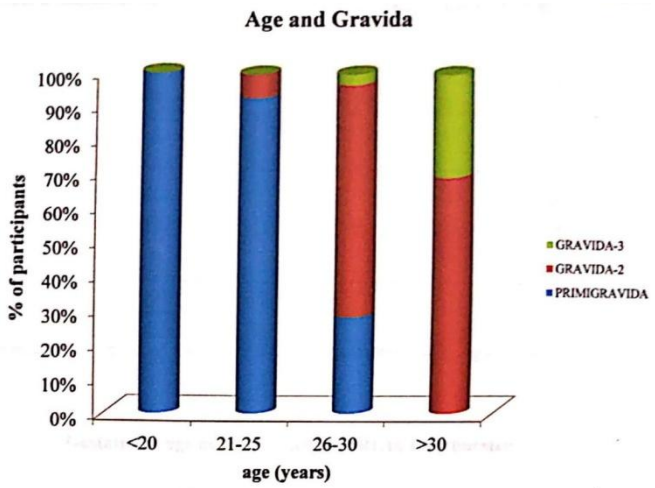
Table 2: Parity distribution of the study population

PARITY	Frequency	Percentage (%)
Primigravida	61	61.0
Gravida–2	34	34.0
Gravida–3	5	5.0
Total	100	100.0

Chi-square for trends: χ^2 value= 47.06, df=2, ***p* value< 0.001**, highly significant

There was a significant difference in the parity distribution of the study participants as most of the participants were primigravida (61%) whereas the multigravidas were less (39%).

Figure 1: Age and gravida distribution of study population



The parity increased as the age of the patient increased as is evident from the above graph. Those above 30 age group had multigravida status whereas the younger ages were more of primigravida. The above distribution was obtained after the mothers with multiple pregnancies and complicated labour or abnormal births were excluded from the study.

There was a significant difference in the distribution of average gestational age as determined by CRL among the study participants as most of the participants were at 33-36 weeks of gestation (47%). The study included measurement of intra-uterine anthropometry of the foetus only in the third trimester of pregnancy.

Table 3: Distribution of average gestational age as determined by TCD

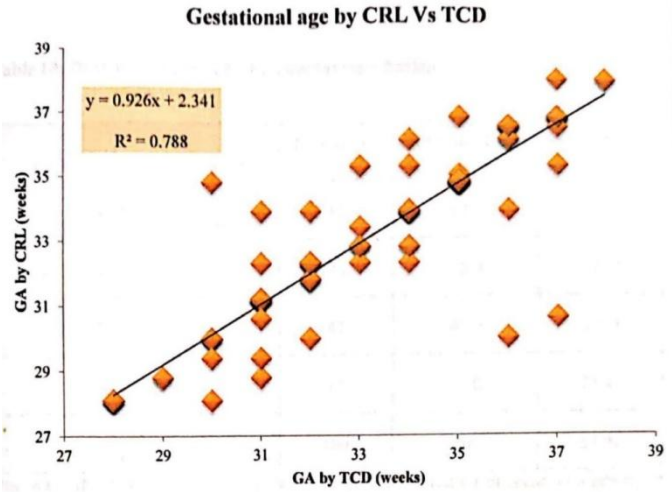
TCD-Gestational age (in weeks)	Frequency	Percentage (%)	Mean TCD(mm)	SD
24-28 Weeks	12	12.0	35.17	3.1
29-32 Weeks	28	28.0	37.68	2.5
33-36 Weeks	47	47.0	45.04	2.8
37-40 Weeks	13	13.0	50.31	1.9
Total	100	100.0	42.48	5.6

One way ANOVA test: F=112.87, p< 0.001, significant variation of mean TCDs among

The TCD obtained ranged from a mean of 35.17 mm at 24-28 weeks to 50.31 mm at 37-40 weeks of gestation, the latter being the TCD for a term

foetus. The standard deviation was 45.04 ± 2.8 at 33-36 weeks of gestation.

Figure 2: Correlation of GA in weeks by CRL and TCD



The above graph shows that the gestational age as determined by CRL in first trimester correlated significantly [p<0.001] with the gestational age as determined by TCD in the third trimester. This shows that TCD can be reliably used to calculate gestational age.

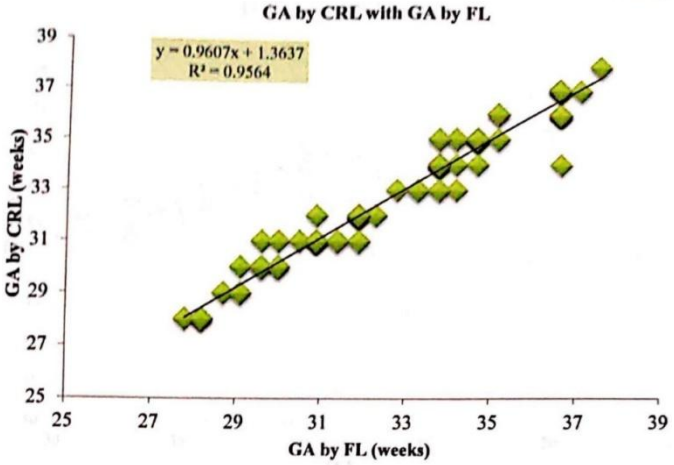
Table 4: Distribution of average gestational age as determined by FL

FL-Gestational age (in weeks)	Frequency	Percentage (%)	Mean FL(mm)	SD
24-28 Weeks	12	12.0	56.92	3.4
29-32 Weeks	28	28.0	59.82	2.2
33-36 Weeks	47	47.0	68.11	2.4
37-40 Weeks	13	13.0	72.46	0.8
Total	100	100.0	65.01	5.7

One way ANOVA test: F=166.7, **p<0.001**, significant variation of mean FLs among the

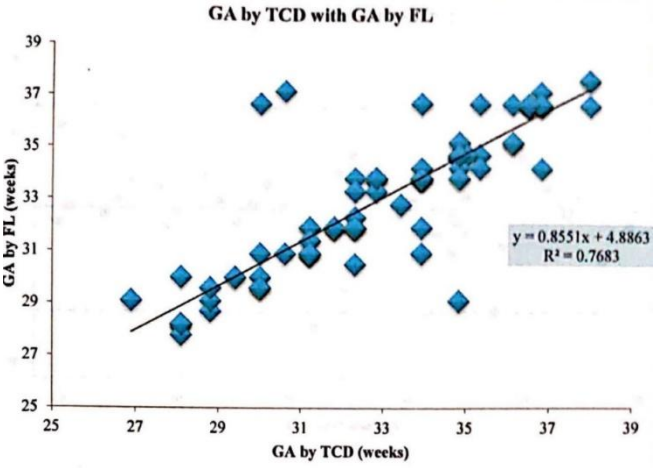
Most of the FL (39%) were evaluated at 33-36 weeks of gestation The FL obtained ranged from a mean of 56.92 mm at 24-28 weeks to 65.01 mm at 37-40 weeks of gestation, the latter being the FL for a term foetus. The mean and standard deviation was 72.46+ 2.4 at 33-36 weeks of gestation.

Figure 3: Correlation of GA in weeks by CRL and FL



The above graph shows that the gestational age as determined by CRL in first trimester correlated significantly 1p<0.001] with the GA by FL in the third trimester. This shows that FL can be reliably used to calculate gestational age.

Figure 4: Correlation of GA in weeks by TCD and FL



The above graph shows that the gestational age determined by trans-cerebral diameter (mm) correlated significantly [p<0.001] with the gestational age determined by Femur Length (mm) in the third trimester. This shows that TCD and FL can be reliably used to calculate gestational age individually and are equally reliable.

Figure 5: Ultrasound Measurement of TCD

Discussion

The present study was done among 100 normal singleton pregnant mothers with normal foetal growth pattern attending to the Department of Radiology, AMC for sonographic evaluation (or as a part of antenatal health check-up) referred from the Department of Obstetrics and Gynaecology.

The mean TCD measured in the present study was 35.17±3.1mm at 24-28 weeks of gestation. This was higher compared to the mean TCD done by Mustafa Z. Mahmoud et al.[9] which documented the mean. TCD as 28.6 ±7.5 mm. The study was done among 50 pregnant women with LMP determined the gestational age ranging from 15 to 37weeks. This study included all the trimesters whereas the present study was done only among third trimester pregnant women.

The mean TCD (in mm) in different gestational age groups was 35.17±3.1mm, 37.68±2.5 mm, 45.04±2.8, 50.31±1.9 mm at 24-28 weeks, 29-32 weeks,33-36 weeks and 37-40 weeks respectively. There is an increasing trend in the mean TCD as the gestational age (in weeks) increases in the third trimester.

In the study done by Charusmita Agrawal et al.[10] the mean age of the women was 24.82 + 3.31 and 85% women were in age group 21-30. The mean TCD in 20-28 weeks was 24 ± 3.86 mm and in 30-36 weeks was 39.31 ± 2.51mm. Median TCD increases from 20.35 mm at 20 weeks to 41.7 mm at 36 weeks of gestation. Both the above studies did not include IUGR foetuses. The normal growth pattern of the foetus was ensured before determining the mean TCDs. The cerebellum being non-subjective for variations during intra-uterine life shows a linear growth pattern throughout pregnancy. The third trimester TCD values were slightly higher in the present study compared to the previous studies. But the difference was not high to show the difference in inferences of gestational age.

Gupta AD et al.[11] observed the gestational age of singleton pregnant women who were not sure of their LMP reliably estimated by measuring the TCD (Trans-Cerebellar Diameter) in mm which showed good correlation with gestational age ($r=0.946$, $p<0.001$). Assessment of the development of the cerebellum was done using the increasing trends in TCD. The similar documentation was done in our study where LW' was subjected to more recall bias where TCD came as a rescuing remedy.

Naseem F et al in their study measured TCD and I3PD and correlated with gestational age determined by LMP. In this study, they observed that in 228 patients, when compared with GA by LMP, TCD had given accurate gestational age in 209 patients and BPD had given accurate gestational age in 176 patients[12]. In the present study the proportion of the participants who had knowledge about LMP was less. The LMP correlated gestational age showed lower predictive value compared to TCD which was the reason to adhere to CRL measured in first trimester of pregnancy.

The present study excluded IUGR babies and those with detected congenital anomalies. The biometric diameters are suggested not be used in case of anomalies because of variabilities in neural infrastructure morphologically. Trans-cerebellar diameter is shown to have less morphological variations even in cases of congenital malformations of the cranium and anomalies.

Rotmensch S. et al[13] conducted a study measuring the TCD in cases of Down's syndrome

documenting that the cerebellar diameters in such affected foetuses were lesser than normal controls at all gestational age by an average of 0.67-0.87 mm. An observed to expected cerebellar diameter ratio of 0.92 was calculated for a sensitivity of 21%, specificity of 95% and PPV 1.66% and 0.50% in a population with risk of having Down syndrome of 1 in 250 and 1 in 750 respectively.

In the present study, the correlation between gestational age as determined by CRL in first trimester and Femur length (FL in mm) values in the third trimester was highly significantly [$p<0.001$] ($r = 0.975$). This was exactly similar to the previous study showing a more reliability and consistency of FL in judging the gestational age.

The study done by Goldstein et al.[14] documented the parameters about 371 women who were at their 13-40 weeks gestational period. Various biometric parameters like occipito-frontal diameter, BPD and TCD found strong curvilinear relationships viz: gestational age and TCD ($r2= 0.948$; $p = 0.0001$), TCD and BPD ($r2 = 0.956$; $p = 0.0001$), TCD and HC ($r2 = 0.969$; $p = 0.0001$). The study found relationships between gestational age determined at first trimester and other parameters similar to our study. But the sample size was higher compared to our study. Yet the present study was able to achieve the correlation values similar to the previous study which further establishes the authenticity of the results obtained in our study.

The cerebellar measurements in the posterior fossa arc not subject to modifications when the growth pattern of the foetus was disturbed. Various studies done on IUGR children documented that TCD can be used as a reliable marker for foetal morphological and neural development.

Hata et al.[15], in their study on 116 pregnant women with foetal head anomalies, stated that TCD is more reliable indicator for predicting the accurate gestational age in case of brachycephaly or dolichocephaly and other rare congenital disorders. They achieved a strong correlation between the TCD and gestational age ($r = 0.96$; $P < 0.001$). However, in our study, there were no cases of any neural tube defects.

Thus, there is an added advantage about TCD, which was documented in the above study and reassured subsequently in the other studies that the case to case variability based on the rate and pattern of growth of the foetus in vivo was less observed in TCD compared to the other foetal biometric parameters.

Vinkesteijn et al.[16], in 2003, studied pregnancies associated with growth restriction and documented that the TCD linearly ascends with advancing gestational age in the normally developing foetus. An exceptional increased TCD/AC values were related to foetal intra-uterine growth restriction. There was a twofold increase in the perinatal mortality among the growth-restricted foetuses with a smaller cerebellum compared to that encountered with the other normal foetuses.

Maliket al.[17] in his compilation of results stated that the trans cerebellar diameter in the third trimester increased in a linear fashion, while trans cerebellar diameter/abdominal circumference (TCD/AC) ratio remained constant throughout the second half of pregnancy. All the parameters were expressed by regression equations and correlation coefficients were found to be statistically significant.

In our study there was a linear increase in the mean TCD values as the gestational increased in the third trimester. As per the previous study the scope to determine the TCD/AC ratio was not available in our study as the objectives of the study never pertained towards measurement of abdominal circumference. But the linear progressive increase of TCD as per the GA gives a full proof of the reliability of TCD in estimating the GA in the third trimester and is not anyway related to the rate of growth of the child. In fact, if the scope of research is expanded to find a correlation between the birth weight of the new-born of the followed up pregnancies and TCD intra-uterine, it would clearly say that TCD can be an isolated parameter for GA compared to other

parameters which are subject to variation due to growth of the child.

The mean FL in our study was 68.11±2.4 nun at 33-36 weeks of gestation. The mean H. values at 24-28 weeks, 29-32 weeks,33-36 weeks and 37-40 weeks were 56.92± 3.4 mm, 59.82 ± 2.2 mm, 68.1 ± 2.4 mm and 72.46±0.8 mm respectively.

Similar results were observed by Uikeyet al.[18] who documented the relationship between gestational age and Femur length (r2 = 0.976). As documented early the study showed very strong correlation between TCD and FL determined gestational age also. There is an increasing trend in the parameters as the GA increases. The length of the femur diaphysis is not subject to much external variations or confounders and only varies with time. Gender differences in femur length have not been studied but the variations shall not be of paramount significance as far as it is in vivo.

Femur length and Trans-cerebellar diameter have been relatively equally efficacious in predicting the gestational age. If the real inference of these parameters is explored, TCD variations infer variations in neural growth or brain development and FL variations can infer bone growth or linear physical growth of the foetus. A combination of these two factors connected by a linear equation will be useful determinant of gestational age. Based on linear regression model applied for variables in the present study, the gestational age can be determined using the following equation:

GA (in weeks) = 5.804* + 0.99 (TCD in mm) + 0.36 (FL in mm)

*Constant derived from the linear regression model

The predictive value of the above equation needs further exploration in wider sample frame studies. Further the dependent variable in this linearity is based on CRL determined gestational age which is taken as standard for the study.

The present study observed a good concordance between the femur length and the trans-cerebellar diameter in predicting the gestational age. The gestational age determined by trans-cerebral diameter (mm) correlated significantly [r2= 0.87, p<0.001] with the gestational age determined by Femur Length (mm) in the third trimester. The trans-cerebral diameter (mm) directly correlated significantly [r2= 0.958, p<0.001] with the Femur Length (nun) in the third trimester.

Conclusion

- The study estimated the TCD and FL values in different gestational ages in the third trimester of pregnancy among normal singleton pregnant women.
- There was significant correlation of the TCD and FI, values measured in third trimester with gestational age determined by CM, in the first trimester.
- TCD and FL showed positive correlation during the third trimester of pregnancy.
- TCD and FL can both be individually used as reliable intro-uterine fetal biometric parameters in estimating the gestational age during the third trimester of normal pregnancy.

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