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Foetal Transcerebellar Diameter (TCD) measurement between 18 and 23 weeks of pregnancy

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Abstract

Background: The measurement of the Transcerebellar Diameter (TCD) is an emerging ultrasound parameter useful for the estimation of gestational age (GA).
Objectives: The objectives of the present study included the establishment of baseline TCD values between 18 and 23 weeks of pregnancy, as a basis for predicting gestational age. Other targets included the determination of the correlation between TCD and the actual/predicted gestational ages and the concordance between the actual and predicted gestational ages in the population.
Methods: A cross-sectional study was conducted on 488 singleton fetuses during the second-trimester anomaly scan sessions. Transabdominal ultrasound scan measurement of the Transcerebellar Diameter (TCD) was carried out using standard criteria and both TCD, and GA measurements were used to construct nomograms. Chi-square (Goodness-of-fit) was used to evaluate the statistical significance of differences between the observed and expected (predicted) TCD and GA values. The actual gestational age subtracted from predicted gestational age was subjected to Pearson correlation to determine concordance (r).
Results: Transcerebellar Diameter ranged between 16.7mm at 18 weeks and 26.7mm at 23 weeks, with a mean value of 18.5$\pm$ 0.96mm and 23.1 $\pm$1.65mm respectively. There was a positive correlation between TCD and GA (r = 0.85; p<0.0001). Concordance between the actual and predicted gestational age was high (Pearson correlation r = 0.81; p < 0.0001).
Conclusion: The TCD is a reliable marker for gestational age estimation between 18 and 23 weeks of gestation.

Keywords: Antenatal care; Concordance; Correlation analysis; Gestational Age; Regression analysis; Transcerebellar Diameter.

Introduction

Gestational age estimation is one of the important decisions which guide care during pregnancy. It is the basis for the appropriate timing of deliveries and

management of complications. Studies have shown that decisions based on inaccurate gestational ages result in higher foetal and maternal morbidity and mortality. [1, 2] The traditional method of estimating gestational age, which is based on the last menstrual period, could be influenced by the regularity of menstrual cycles, especially in the immediate three months pre-conception and also by prior exposure to hormonal contraception. In women from developing countries, late antenatal booking, the absence of accurate menstruation records and menstrual cycle irregularities are additional challenges. [1, 3, 4, 5]

Sonographic estimation of gestational age is the 'gold standard' in antenatal care, with the first-trimester measurement of crown-rump-length (CRL) which is considered the most reliable index. [6] However, most pregnancies are booked after the first trimester, in many developing countries where the lack of proper recording of menstruation dates further contribute to the challenge of accurate gestational age estimation.[3 - 5] The most frequently used foetal biometric parameters after the first trimester include the biparietal diameter (BPD), femur length (FL) and abdominal circumference (AC). [1, 5] Nevertheless, the reliability of these biometric methods could be affected by extrinsic factors such as alteration in the shape of the foetal head (as it occurs in breech presentation and hydrocephalus) and abnormalities of the long bones such as achondroplasia. [1]

A less commonly used parameter is the Transcerebellar Diameter (TCD), which was fortuitously found to be a useful parameter for determination of GA, while it was being evaluated for the assessment of foetal cerebellar growth and its disorders. The foetal cerebellum in the embryo appears at the end of 5th week of pregnancy and can be reliably measured using ultrasonography from the 12th to 14th week of gestation till delivery. [1, 7, 8] The anatomical location of the cerebellum in the posterior cranial fossa makes the organ less vulnerable to external pressures on the foetal cranium. [1, 9] Studies of TCD shows that the cerebellum is the least organ affected by foetal growth abnormalities and also revealed its potential for reliable estimation of gestational age. [1, 9]

Ultrasonographically, the cerebellum, in the second trimester, can be easily viewed as a central rectangular echogenic structure (vermix) connecting two oval echoluscent structures (hemispheres) after the 14th week of gestation. [1, 10] With minimum expertise, the measurement of TCD is reproducible. Foetal transcerebellar diameter (TCD) which is an emerging parameter for gestational age estimation has only been evaluated among Nigerian pregnant women in few studies. [11, 12] The objectives of the present study included the following: to establish baseline TCD values between 18 and 23 weeks of pregnancy for accurate prediction of gestational age, to determine the correlation between TCD and the actual/predicted gestational ages and to determine the concordance between the actual and predicted gestational ages in a Nigerian population.

Methods

This survey used a cross-sectional design, and it was conducted on 488

uncomplicated singleton gestations between 18 and 23 weeks of pregnancy. It involved collaboration between the Foetal Medicine Units of the Department of Obstetrics and Gynaecology, Olabisi Onabanjo University Teaching Hospital, Sagamu and High Rocks Foetal Medicine Centre, Lagos, Nigeria, between 1st June 2015 and 31 March 2016. Ethical approval was obtained from the Health Research Ethics Committee of Olabisi Onabanjo University Teaching Hospital, Sagamu and signed written informed consent was obtained from all the participants after explaining the purpose of the study.

Only pregnancies that were conceived after normal menstruation and those in whom the last menstrual period (LMP)-derived gestational age (GA) was validated by a first-trimester scan were included in the study. The LMP- derived GA was considered validated and used only when it was < 7 days different from USS-derived GA. Foetuses with congenital anomalies, irrespective of the aetiology and disorder of growth such as suspected intrauterine growth restriction, were excluded. A transabdominal ultrasound scan was done in all cases using 3.5 - 5.0 MHz sector transducer on Sonoscape S20 and Voluson P8 ultrasound scan machines. All scans procedures were performed by two sonologists, while images and accuracy of measurements were validated by a single physician (certified by the Foetal Medicine Foundation, London) to reduce Inter-observer variability. The Intra-observer error was reduced by using the average of three measurements from three images.

The transventricular or transverse axial plane defined by the appearance of 'arrow-like' image of central midline echo intercepted in the anterior third by the cavum septum pellucid and the frontal horns of the lateral ventricles (feathers) was first identified. The transducer was slightly rotated (~30°) from this plane to get the transcerebellar plane that was used to acquire the image of the cerebellum. The measurement was made in plane showing the cisterna magna (CM) and nuchal fold (NF), with callipers placed 'out- to – out' on the margin of the widest diameter of the cerebellum (Figure 1).Complete foetal anatomical scan was done in all the patients as the primary indication for referral.

Data interpretation and statistical analysis

The GA in weeks derived from ultrasound measurements were assigned by approximating additional days above a particular week to the nearest week. Less than four days and above five days were allocated to the lower and higher weeks, respectively. [13] Measurements were further converted to variables and units that could be analysed with SPSS statistical software, where necessary. *P* values < 0.05 were considered statistically significant.

Simple linear regression models constructed separately for the mean were used to develop a nomogram for transcerebellar diameter (TCD) and gestational age (GA). Regression equations were further used to estimate the predicted TCD 5th, 50th and 95th centiles for each GA as well as the predicted GA 5th, 50th and 95th centiles for each TCD measurement (Table II). The 50th centile of the TCD and GA were adopted as observed data, while the

predicted values in both parameters were used as expected values in the study. Based on these, Chi-Square ($\chi 2$) (Goodness of fit) test was used to evaluate the statistical significance of the difference between the observed and the expected TCD and GA. Results were considered significant at $P< 0.05$.Using week and day unit, the concordance between the actual gestational age (AGA) and predicted gestational age (PGA) was assessed using the Pearson's correlation coefficient (r), after subtracting the actual gestational age (AGA) from the predicted gestational age (PGA) values.

Figure 1: USS Image of Transcerebellar Diameter of foetus at 18-23 weeks

Results

Four hundred and eighty-nine pregnant women fulfilled the inclusion criteria and were studied. However, the TCD was visualised, and images appropriate for measurements were obtained among 488 (99.7%) fetuses. The gestational age distribution showed that 118 (24.2%) women had their ultrasound scan at 21 weeks, while 62 (12.7%) had an ultrasound scan at 18 weeks (Figure 2).
The TCD and GA measurements between 18 and 23 weeks were analysed as shown in Table I. The mean TCD at 18 weeks was 18.5±0.96mm with a range of 16.7mm and 19.4mm while at 23 weeks, the mean TCD was 19.9±1.65mm with a range of 23.1mm – 26.7mm (Table IA). In Table IB, the mean GA was 18.5 ±0.16 weeks and a range of 18.0 weeks - 20.0 weeks at TCD measurement of 18.0mm. At TCD of 23mm, the mean GA was 23.5 ± 0.19 weeks while the range was 20.0 weeks - 24.4 weeks. A positive linear correlation was observed between the TCD and increasing GA ($r = 0.85$; $p< 0.0001$) (Table I).

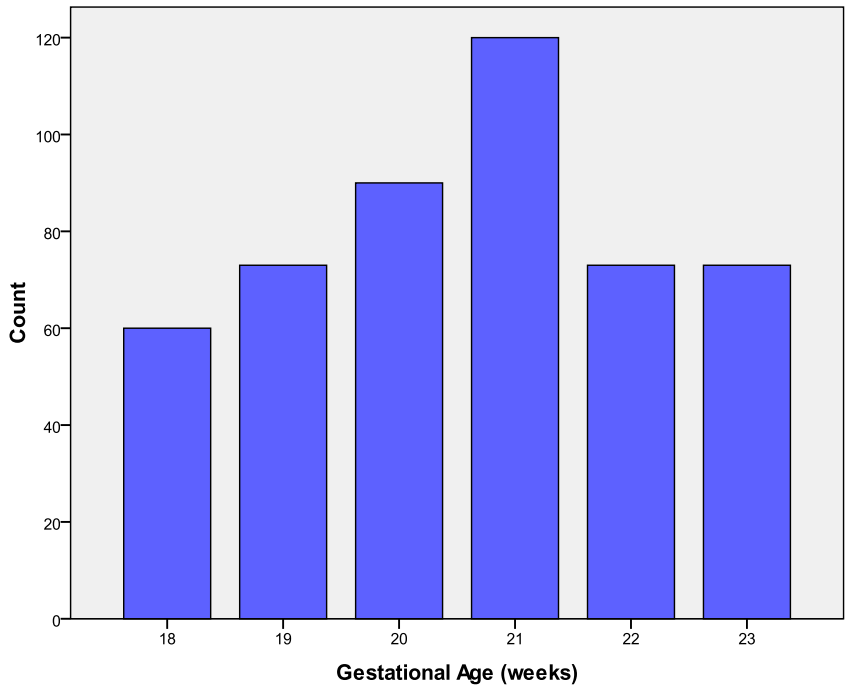

Figure 2: Distribution of subjects according to the Estimated Gestational Ages in weeks.

Table I: Baseline Parameters of the TCD and GA

Weeks	Number	Mean	SD	Minimum	Maximum
A. Gestational Age (weeks)	(n = 488)			Transcerebellar Diameter	
18	62	18.5	0.96	16.7	19.4
19	77	19.0	1.57	17.4	22.4
20	92	19.6	1.29	18.1	23.5
21	118	21.4	1.51	19.3	25.2
22	73	21.9	1.32	19.6	24.1
23	70	23.1	1.65	19.9	26.7
B. Transcerebellar Diameter (mm)	(n = 488)			Gestational Age	
18	55	18.5	0.16	18.0	20.0
19	118	19.0	0.11	18.2	21.5
20	127	19.6	0.17	18.0	22.8
21	88	20.6	0.02	19.1	23.0
22	51	22.0	0.20	19.6	24.0
23	49	23.5	0.19	20.0	24.3

SD – Standard Deviation

Table II: Regression Equations for TCD and GA

Parameters	Regression Equation
TCD	TCD_{Mean} = -13.5 + 1.70*GA
GA	GA_{Mean} = -7.51 + 1.40*TCD

TCD – Transcerebellar Diameter; GA - Gestational Age

The regression equation models in Table II were used to calculate 5th, 50th and 95th centiles for TCD obtained from GA values and GA from TCD values (Table III).The predicted TCD for each GA was closer to the 50th centile between 18-20 weeks than between 21-23 weeks (Table III). The statistical analysis (Table IIIA) showed that the differences were not statistically significant in both groups ($\chi2$ = 0.061; p = 0.082 and $\chi2$ = 0.013; p = 0.867). In Table IIIB, the predicted GA was also closer to the 50th centile between 18-20 weeks than between 21-23 weeks (Table III). These differences were however not statistically significant in both groups ($\chi2$ = 0.034; p = 0.052 and $\chi2$ = 0.462; p = 0.424)

The concordance between the actual and predicted GA, described in Table IV, revealed that there was a strong positive correlation between the actual and the predicted GA (Pearson correlation, (r = 0.86; p < 0.0001). On the average, there was no difference between actual and predicted GA within 18-20 weeks, while a gap of 7 days was observed between 21-23 weeks gestation period.

Table III: Predicted GA and TCD between 18 and 23 weeks

A. Predicted Transcerebellar Diameter					
Gestational Age (weeks)	Transcerebellar Diameter (mm)				
	5th	**50th**	**95th**	**Predicted**	**Statistics**
18	16	18	24	17.1	
19	16	19	25	18.8	χ^2 = 0.061
20	17	20	23	20.5	P = 0.082
21	18	22	26	22.2	
22	19	23	27	23.9	χ^2 = 0.136
23	19	24	28	25.6	P = 0.867
B. Predicted Gestational Age					
Transcerebellar Diameter (mm)	Gestational Age (weeks)				
	5th	**50th**	**95th**	**Predicted**	**Statistics**
18	17.0	18.3	19.6	17.9	χ^2 = 0.034
19	18.1	19.1	20.6	19.1	P = 0.052
20	18.5	19.6	21.5	20.5	
21	19.3	21.0	22.2	2.9	χ^2 = 0.462
22	20.0	21.3	22.7	23.3	P = 0.424
23	20.3	22.2	23.2	24.7	

Discussion

The assessment of growth of the foetal cerebellum throughout gestation has been advocated since 1986. [7] One of the early studies by Campbell *et al*., reported the superior advantage of TCD measurement over the traditionally used parameters for GA estimation, in particular between 12 and 18 weeks based on the LMP. [13] Other studies in the literature have also established the TCD as a unique and reliable parameter for estimating gestational age between the 14th and 42nd week of pregnancy. [1, 7, 15, 16] Our study was conducted during the second trimester of gestation, and the findings are suggesting that the measurements between 18 and 23 weeks are reliable in estimating GA.

The TCD is mostly gaining acceptance as a reliable tool for estimating GA because it is not influenced by abnormalities of foetal growth such as intrauterine growth restriction, shape of the foetal cranium or multiple pregnancy and neither has any adverse safety issues, related to the use of ultrasound scan at this gestational period, been documented. [1, 9, 17] The uniqueness of the present study is that it was conducted in a dedicated foetal medicine unit, between 18 and 23 weeks of gestation, with particular attention to measures that reduced both Intra-observer and Inter-observer variability. In addition, to the best of our knowledge, previous studies available to us were not specifically conducted between this gestational age intervals. [8, 11, 16]

Table IV: Concordance between AGA and PGA based on TCD measurements

	Mean GA (weeks/day)		
TCD (mm)	**Actual**	**Predicted**	**Difference**
18	18/0	18/0	0/+0 (+0 Day)
19	19/3	19/2	0/-1 (-1 Day)
20	20/3	20/4	0/+1 (+1 Day)
21	21/5	22/1	0/+3 (+3 Days)
22	22/0	23/1	1/+1 (+8 Days)
23	23/1	24/3	1/+2 (+10 Days)

Note: Data interpreted in Week/Day

The Intra- and Inter-observer variability in our study was better than the variability of 3.8% and 3.6% reported in a similar study. [7] Although the findings of the present study corroborated the previous findings which demonstrated a linear relationship between TCD and GA. The additional yield from the current study was the direct correlation which was optimal at 18 to 20 weeks than at 21 to 23 weeks. This observation was based on the differences between the actual and predicted GA at a given TCD measurement that was shown to be farther apart between 21and 23 weeks GA period. [11, 19] A similar finding was reported in India where correlation between TCD and GA became weaker after 20 weeks GA. [1] Some of the other previous studies compared the TCD and GA relationship across second and third trimesters of pregnancy. [7, 16]

Another striking finding from the present study was the relationship between the actual and predicted GA. This difference was prominent between 21and 23 weeks of gestation. The difference between the findings of the present study and some previous studies may be partly explained by the fact that the **n**umber of pregnancies studied within the 18 to 23 weeks GA period was comparatively larger in the present study, as well as the fact that strict guidelines were used to reduce Inter-observer errors. [1, 18] The antenatal population used was often below 100 women in some of the studies reviewed while a much larger population was studied in fewer studies such as the study reported by Charvez *et al*. [1, 7, 17, 18] The study also reported widening of the difference between actual and predicted GA with increasing GA, being nine days at 37 weeks of gestation. [9] In the study done among Indian antenatal population, only 23 women were evaluated in the second trimester, while in Netherlands study, the effect of chromosomal abnormality was found to affect the TCD measurement. [1, 18] The sample size for our study improved the scientific significance of study inferences.

Conclusion

The findings of the present study offered normal ranges of TCD between 18 and 23 weeks of pregnancy and also demonstrated a strongly positive linear relationship between TCD and GA. Consequently, TCD appears a reliable marker for GA estimation at this period of gestation in particular between 18 and 21 weeks and we recommend it for everyday application in our local practice.

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Authors' Contributions: OOA, STO and MA conceived and designed the study while ultrasonography was performed by OOA and AM. All the authors analysed the data and drafted the manuscript.

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