Cerebellar Measurements with Ultrasonography in the Evaluation of Fetal Age

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Abstract: *The use of ultrasonography has significantly improved the evaluation of fetal growth and development and has permitted prenatal diagnosis of a variety of congenital malformations.Campbell et al in (1968) studied fetal cephalometry in the second trimester and determined that the fetal head can be measured from 13th week of pregnancy².*
BinholzJ.C(1982) studied the new born cerebellar size both in full term and in preterm babies.
To estimate the gestational age of the fetus by measuring transcerebellar diameter in normal and Intrauterine growth retarded pregnancies by ultrasonography and to evaluate whether the transcerebellardiameter or other parameters like biparietal diameter, head circumference, abdominal circumference is accurate for the gestational age.

Aims and Objective:
  ➢ *To evaluate the usefulness of transcerebellar diameter as against the conventional parameters of biparietal diameter and femur length in normal pregnant mother between 15 to 40 weeks.*
  ➢ *To evaluate the usefulness of transcerebellar diameter in antenatal diagnosis of intrauterine growth retardation.*
  ➢ *To derive nomograms for estimating the gestational age of the fetus from the measured transcerebellar diameter.*
  ➢ *To evaluate morphological abnormalities.*

Method: *Ultrasonographic estimation of gestational age by transcerebellar diameter was done in normal and intrauterine growth retarded pregnancies in 100 pregnant women(80 normal pregnancies and 20 IUGR pregnancies) between 15 to 40 weeks of gestation.*

Result: *The study was conducted in the department of radiodiagnosis in Adichunchangiri Institute Of Medical Sciences.Out of the 100 patients who were scanned for the trabscerebellar diameter and other parameters- biparietal diameter, head circumference, abdominal circumference and femur length 80 were of normal pregnancies and 20 were with intrauterine growth retardation. The results obtained were that the patients with normal pregnancy and those with IUGR had no statistically difference with the age and parity. It showed that in 17 out of 20 patients the TCD measurements were within the normal range(between 5th and 95th percentile) and only in 3 patients it was less than 5th percentile but BPD and FL were less than 5th percentile in 18 out of 20 patients and AC,HC measurements were less than 5th percentile in all the 20 patients. This difference was statistically significant(P=0.0001),that is TCD measurements were within the normal range in significantly higher number of patients than other ultrasonic measurements.*

Conclusion: *Transcerebellar diameter is the better parameter for gestational age assessment than BPD and FL as it is not fraught with the problems in the measurements commonly encountered in BPD and FL and also it is an added advantage in cases of IUGR pregnancies and also can be used as a single growth parameter to predict the gestational age using various obtained formulas and nomograms both in normal and IUGR pregnancies*

Key Words: *Cerebellar measurements, Ultrasonography, Fetal age.*

I.   Introduction:

Increased diagnostic capability to identify multiple structural lesions with in the fetus has many implications. Early diagnosis of a congenital anamoly with a hopeless prognosis allows for termination of pregnancy. Detection of a less severe defect or late termination of severe malformation may alter the subsequent obstetrical course. Caesarean section may be indicated when continued intrauterine existence is detrimental to the fetal well being. Some malformation may be followed to a normal term delivery with subsequent extra uterine evaluation and therapy.

One of the commonest problems that an obstetrician faces frequently is the estimation of fetal maturity for the purpose of either prolonging pregnancy or when the termination of the purpose of either prolonging pregnancy or when the termination of pregnancy is being considered for such complications as pregnancy

induced hypertension,diabetes and Rh disease.The means that are widely accepted for estimating fetal maturity are:-
1.Gestational age
2.Weight of the fetus

The methods for assessing the fetal age[6]
1.Assessment by estimating the size of the uterus especially between 8 and 24 weeks of gestation.
2.Average duration of pregnancy 266 days from conception and 280 days from date of last menstrual period in women with 28 days cycles
3.Naegele 's rule:To add 7 days to the first day of last menstrual period and to count back 3 months.
4.Mac Donald rule:The height of the fundus is measured by a flexible tape and duration of pregnancy calculated from:
-Height of fundus(in cms)x2/7=duration of pregnancy in lunar months(or)
-Height of fundus(in cms)x8/7=duration of pregnancy in weeks.
5.Date of quickening:If this can be ascertained definitely,22 weeks should be added to date of quickening which gives probable date of confinement.
6.Abdominal girth measurements:Size of the head,degree of mobility and the width of the sutures and fontanels.
7.The state of the cervix.

X-ray estimation of gestational age:
a)Development of ossification centres is as follows:
There are several ossification centres in fetal bones.The chronological order of the appearance of the ossification centres is as follows:

Ossification center	Time
1.Calcaneum	24-26 weeks
2.Talus	26-28 weeks
3.Distal Femoral Epiphyses	33-35 weeks
4.Proximal Tibia	36-38 weeks
5.Proximal Femoral	38-40 weeks
6.Capitate,Hamate	40 weeks

The presence of certain bone centres is a sure indication of fetal maturity. Fetus in whom proximal tibial epiphysis and distal femoral epiphysis is visible antenatally are seen definitely mature at birth. The center of corresponding bones on the opposite side should be visualised. Normally they should be symmetrical and of equal size. A significant degree of asymmetry of the centers is highly suggestive of a congenital anamoly. In particular to the knee joint. Since these appearance coincides with the beginning of growth problem in a fetus.

Dental Development
It is a reliable index of full term maturity.1st Molar becomes radiographically visible at 32-33 weeks and 2nd molar at 36-38 weeks. The maturation of tooth is not affected by the condition,which affect the growth of other structures in utero such as cretinism where ossification of the distal femoral and proximal tibial bone centers is absent even beyond 40 weeks of aged.The other methods used to estimate gestational age are:
1.Fetal head size
2.Crown breech measurement
3.Fetal fat line ratio
4.Placental calcification
5.Cytological examination and biochemical of liquor amni
It is well established that prematurity is the leading factor associated with neonatal morbidity and mortality.Hence to estimate prematurity,prediction of fetal gestational age is of utmost importance.
Presently it appears that the most effective way to date pregnancy is by the use of ultrasound examination. Several sonographically derived parameter now available can be used to date pregnancies which include the BPD,FL etc of the significance is the fact that the ability to estimate the gestational age by most of these measurements is to be a lesser extent towards the correct value after 26 weeks of gestation.To avoid these problems in the circulation of fetal age, transcerebellar diameter by ultrasonic technique to calculate the gestational age has been found to be highly significant and not fraught with the above mentioned difficulties and it can be used to reliably approximate gestational age in foetuses affected by intrauterine growth retardation.

II. Materials And Methods:
Study Design:This study of ultrasonographic estimation of gestational age by transcerebellar diameter in normal and intrauterine growth retarded pregnancies was conducted on 100 pregnant women(80 normal pregnancies

and 20 IUGR pregnancies).These 100 women were recruited into the study from antenatal clinic (OPD) and in patients admitted (IP) into Adichunchanagirihospital,B.G.Nagar. A total number of 100 scans were performed between 15 and 40 weeks out of which 80 were in the group unassociated with any medical disorder and 20 were in the group of intrauterine growth retarded pregnancies.

Inclusion Criteria:Normal pregnancies between 15 and 40 weeks of singleton pregnancies with known last menstrual period, Clinically suspected intrauterine growthretardation.

Exclusioncriteia: Multiple pregnancies**,**Congenital malformations**.**

Equipment: The USG machine "Voluson S6 Pro" from GE(3D)with a transducer of 5 MHz was used during the study.

Examination Method: An informed consent from all the patients was taken and the patients were explained about the atraumatic nature and significant diagnostic importance of the procedure,which is being performed.Examination was performed with patient in the supine position,After taking a brief history,obstetrical examination was done;blood pressure was recorded in the recumbent position.Fundal height was measured in the supine position with empty bladder.An ultrasound examination was performed with the patient in the supine position and all parameters were obtained including biparietal diameter,the fetal femur length and the trans-cerebellar diameter. The BPD was taken as cross section parallel to the cantho-meatal line and slightly above it,which includes the falx,thalamus and the most important cavum septum pellucidum and 2/3rds from the occiput,intersecting it in the midline,extending as a line from the anterior to posterior aspect of the skullinterrupted in the mid line by slit like third ventricle and posteriorly by the thalamus.BPD is measured as the largest perpendicular line to the mid line echo,from the midline of the proximal skull to the midline of the distal skull.Fetal femoral length was obtained from the greater trochanter to the middle of the lateral condyle.Abdominal circumference was taken in the plane showing umbilical vein perpendicular to the fetal spine and the stomach bubble.Head circumference was taken in the BPD plane.The trans-cerebellar diameter was obtained by the following methods.The landmarks of the thalamus and the cavumpellucidum and third ventricle were identified.Then by slightly rotating the transducer below the thalamic plane,the posterior fossa was revealed with the characteristic butterfly like appearance of the cerebellum.Thecisterna magna just posterior to the cerebellum.These examinations were performed between 15 to 40 weeks of gestation.

III.   Statistical Analysis:

The measured values were analysed statistically using SPSS 7.5 statistical package for Windows.Students 't' test was used to compare age of the patients between normal age of the patients between normal and IUGR pregnancies.One way analysis of variance (ANOVA) was used to compare parity distribution between the two groups.The ultrasonic parameters TCD,BPD,FL,AC and HC were compared with GA by regression analysis.TCD was compared with BPD,FL.AC and HC using correlation statistics in both normal and IUGR pregnancy groups. Normograms were derived by taking 5th,50th and 95th percentile values in normal pregnancies.The number of patients in IUGR pregnancies whose TCD,BPD,FL,AC and HC measurements were less than 5th percentile for the gestational age when compared with the nomograms derived from normal pregnancies,were analysed by Fischers exact test.P<0.05 was taken significant.

IV.   Results:

The patients with normal pregnancies were aged between 18 to 32 years with a mean±SD of 21.9±3.18years.The patient with IUGR pregnancies were aged between 17 to 30 years with a mean±SD of 22.8±3.38years.There was no statistically difference(P=0.26)between the two groups with respect to age(Table 1).Among the 80 patients with normal pregnancies 45 were primigravida,18 were gravida -3 and 2 were gravida -4.Among 20 patients with IUGR pregnancies 11 were primigravida,5 were gravida -2,3 were gravida -3 and 1 was gravida -4.There was no statistically significant difference between the two groups in regard to parity(p=0.91).(Table 2).From the ultrasonic data obtained from normal pregnancies ,analysis was done to correlate TCD with BPD,FL,AC and HC,which showed good correlation(Table 3). In normal pregnancies,gestational age(GA) was correlated to various ultrasonic parameters including BPD,FL,AC,HC and TCD and a regression analysis was done(Table 4).The analysis showed that the BPD was well correlated to GA(R^2=0.98) and the relationship was curvilinear,best described by a polynomial equation of the second order.

GA=0.0018(BPD)²=0.1554(BPD)+8.5749

FL correlated well with GA(R^2=0.99) and the relationship was curvilinear,best described by a polynomial equation of the second order.

GA=0.0022(FL)²+0.2129(FL)+10.732

AC was well correlated to GA(R^2=0.98) and the relationship was given curvilinear,best described by a polynomial equation of the second order

GA=0.0002(HC)²-0.001(HC)+13.214

Finally the analysis showed good correlation between TCD and GA(R^2=0.98) and the relationship was curvilinear best described by a polynomial equation of the second order

GA=-0.007(TCD)^2+1.1032(TCD)+0.2463

In IUGR pregnancies the gestational age was correlated to TCD and various ultrasonic parameters including BPD,FL,AC and HC(Table 5).There was a very good correlation between gestational age and other parameters including BPD(R^2=0.86),FL(R^2=0.77)and HC(R^2=0.87)

Tables:

	Normal Pregnancies	IUGR Pregnancies	P Value
Age(years) Mean+SD	**21.9+3.18**	**22.8+3.38**	**0.26**

Table 1: Age distribution of NORMAL and IUGR pregnancy patients.

Parity	NORMAL Pregnancies	IUGR Pregnancies
Primigravida	45	11
Gravida-2	18	5
Gravida-3	15	3
Gravida-4	2	1
Total	**80**	**20**

Table 2:Parity distribution of NORMAL and IUGR pregnancy patients

Parameters Compared	R^2	P Value
TCD Vs BPD	0.93	0.0001
TCD VS FL	0.94	0.0001
TCD Vs AC	0.95	0.0001
TCD Vs HC	0.91	0.0001

Table 3:Showing correlation of TCD with BPD,FL,AC and HC in normal pregnancies

Parameters Compared	R^2	P Value
GA Vs BPD	0.98	0.0001
GA Vs FL	0.99	0.0001
GA Vs HC	0.99	0.0001
GA Vs AC	0.98	0.0001
GA Vs TCD	0.98	0.0001

Table 4 :Showing correlation of GA with BPD,FL,AC and HC in normal pregnancies

Parameters Compared	R^2	P value
GA Vs BPD	0.86	0.0001
GA Vs FL	0.77	0.0001
GA Vs AC	0.77	0.0001
GA Vs HC	0.87	0.0001
GA Vs TCD	0.96	0.0001

Table 5 :Showing correlation that is R^2 and P Value GA with BPD,FL,AC,HC and TCD in IUGR pregnancies

	Less than 5th percentile	Within normal range	P Value
BPD	18	2	0.0001
FL	18	2	TCD Vs BPD
HC	20	0	FL,AC,HC
AC	20	0	
TCD	3	17	

Table 6:Showing the number of patients in IUGR pregnancies whose ultrasonic

measurements, when compared with the normogram derived from normal pregnancies,was less than 5th percentile for the gestational age.

Picture showing cerebellar view. The calipers placed on the edges of the cerebellar hemispheres demonstrate the method to obtain trans cerebellar diameter.

Normal pregnancy: picture showing trans cerebellar diameter measuring 28mms at 25 weeks of gestation. The other parameters were BPD – 61mms, FL – 50mms, AC - 208mms, HC – 228mms.

Normal pregnancy : picture showing trans cerebellar diameter measuring 33mms at 28 weeks of gestation. The other parameters were BPD – 67mms, FL – 51mms, AC - 237mms, HC – 262mms.

V. Discussion:

To be of practical value the screening test should be simple and acceptable to the patient and physician. It should have a high degree pf sensitivity and low degree of false positive results. In our study we have scanned eighty uncomplicated pregnancies and twenty intra uterine growth retarded pregnant mothers between 15-40 weeks of gestation. The mean age group for normal pregnancy varies with in the range of 21.9±3.18 yrs and 22.8±3.38yrs in cases of IUGR. There is not much difference in the mean age between normal and IUGR.

Among the 80 patients with normal pregnancies 45 were primigravida,18 were gravida-2,15 were gravida-3 and 2 were gravida-4.Among 20 patients with IUGR pregnancies 11 were primigravida,5 were gravida-2, 3 were gravida-3 and 1 was gravida-4. There was no statistically significant difference between the two groups in regard to parity(p=0.91)

In our study the sonographic visualization of the fetal cerebellum was present as early as 14 to 15 weeks of gestation. The characteristic image of the cerebellum by ultrasonography appears as two lobules on

either side of the midline,located in posterior cranial fossa.Transcerebellar diameter,biparietal diameter,femur length,abdominal circumference and head circumference were measured in all cases to assess the gestational age of the fetus and an attempt was made to detect the correlation between all these parameters and gestational age. An attempt was also made to know correlation between TCD and other parameters. Nomograms for estimating the gestational age from the measured TCD,BPD,FL,AC and HC in normal pregnancies was done.

Stuart Campbell et al(1970) first investigated to link the fetal BPD to the gestational age.He proposed that delivery occurred with in ±9 days of sonar expected date of delivery.

Sabbaga et al then defined the confidence limits of fetal age to the second and third trimester by BPD.In his study he further explained the relation existing between the BPD and duration of pregnancy and showed that prior to 26 weeks of gestation a single BPD can be used to predict the gestational age. But after 26 weeks of gestation BPD vary markedly around these values and are inaccurate indices of fetal age.The growth rate is faster in the earlier period of pregnancy

Hadlock et al worked on elucidating the head shape changes.With the possibility of alteration for fetal head shape including dolicocephaly or brachycepahly ,the criteria for acceptance of BPD for reflecting the gestational age may be wrong.[7]

In our case study we have found a good correlation between BPD and gestational age.

Though the femur length was found to be one of the accurate measurements and many tables were published correlating femur length either with BPD or with the gestational age.Many potential sources of error was found in the technique.In our study we have found that there is a good correlation between femur length and the gestational age.

The above discussion concludes about the uncertainty in the estimation of gestational age,which if further amplified in cases of fetal growth retardation,which are further hampered by lack of precise estimation of gestational age,leading to difficulty in determining whether a fetus is truly retarded,constitutionally small for age or appropriately grown,but with incorrect gestational age.

Pilu et al investigated the ultrasonography of the posterior fossa of the fetus and confirmed the capability of ultrasound to demonstrate the anatomy of the posterior fossa.They suggested that the fetal transcerebellar diameter in utero between 17 and 40 weeks of gestation is more useful indication of accurate gestational age,particularly in case of dolicocephaly and brachycepahaly and also facilitates the antenatal detection of congenital disorders. Micovic et al studies the growth of cerebellum in normal pregnant women and stated that TCD may be practically applied in the gestational age measurement particularly in cases where it is difficult or impossible to measure BPD and in cases where it is unstable due to head moulding,since the cerebellum is not liable to changes particularly inform.[9]

Behman et al studied the regional distribution of blood flow to term primate fetal brain in both control and asphyxiated animals.They found that the blood flow to the cerebellum was significantly higher than that to the cerebral cortex in the control group and in asphyxiated group,although cortical blood flow decreased, blood flow to the cerebellum remained unchanged.In light of these remarkable findings one has to pressure the haemodynamic adjustments observed under experimental conditions are operative in the human fetus and are important in the preservation of normal cerebellar growth in severe fetal growth retardation.[10]

Albert Reece et al studied on nineteen pregnant women with a clinical suspicion of intrauterine growth retardation and with gestational age.Multiple biometric parameters were obtained including the transverse cerebellar diameter.A prenatal diagnosis of intrauterine growth retardation was made in all cases based on the transverse cerebellar diameter being consistently correlated with gestational age as predicted by the last menstrual period,where as most of the other measurements were consistently discrepant by more than 2.5 weeks and the estimated fetal weight of all foetuses was equal to or less than the tenth percentile for the gestational age.They suggested that the growth of transverse cerebellar diameter is unaffected by intrauterine growth retardation.[10]

William.J.Meyer et al prospectively evaluated the accuracy of a gestational age independent method of detecting abnormal growth by transverse cerebellar diameter/abdominal circumference ratio and compared this with standardultrasonographic methods of growth assessment.They concluded that TCD/AC ratio is an accurate gestational age independent method of identifying the small for gestational age but not the large for gestational age infant.[8]

Lyndon et al obtained transverse cerebellar diameter in 44 small for gestational age fetuses between 27-42 weeks.The cerebellar diameter was normal in 12(27.3) between 1-2 SD's,below the mean for gestational age in six(13.6%) and greater than 2 SD's below the mean in 26(59.1/5%).Hence they concluded that transverse cerebellar diameter couln't be used to assess gestational age in those fetuses suspected of being small for gestational age.

The results of our study provide normative data of fetal cerebellar growth through out gestation and demonstrates that the TCD remained unaffected by fetal growth retardation,where as most biometric parameters measured sonographically were significantly affected by the overall growth retardation process.

A linear relationship was found during the second trimester between the growth of the cerebellum measured in mms and the gestational age in weeks.The established normal measurements of the transverse cerebellar diameter through out pregnancy can be used as a standard against which deviation in growth or malformations may be compared and is comparable with other parameters like BPD,FL,HC and AC.Utility of the transverse cerebellar diameter may serve as a relaiable indicator to estimate gestational age in cases of fetal growth retardation.

VI.   Conclusion:

1.Fetalbiparietaldiameter,femurlength,abdominal circumference and head circumference measurements of the fetus in normal pregnancies were comparable with transcerebellar diameter measurement between 15 and 40 weeks of gestation.

2.Estimation of gestational age by transcerebellar diameter correlated with the estimation of the gestational age by other multiple growth parameters.

3.Transcerebellar diameter is the better parameter for gestational age assessment than BPD and FL as it is not fraught with the problems in the measurements commonly encountered in BPD and FL due to its easily identifiable landmarks.

4.Transcerebellar diameter is an added advantage in cases of IUGR pregnancies as it correlates well with the gestational age as compared to other growth parameters.

5.Transcerebellar diameter can be used as a single growth parameter to predict the gestational age using the various obtained formulas obtained and nomograms both in normal and IUGR pregnancies.

6.In addition as observed by Mcleary et al we would like to conclude that,thetranscerebellar diameter should be a routine measurement not only for the estimation of gestational age,but failure to demonstrate the cerebellum could be a sign of Arnold-Chiari malformation or Dandy Walker cyst.

The ultrasonic measurements in the IUGR pregnancies were compared with normograms derived from measurements in normal pregnancies(tables3,4). It showed that in 17out of 20 patients the TCD measurements were within the normal range(between 5th and 95th percentile) and only in 3 patients it was less than 5th percentile but BPD and FL were less than 5th percentile in all the 20 patients.This difference was stastistically higher number of patients than other ultrasonic measurements.

Eighty healthy pregnant women under went routine ultrasonographic examinations and the measurements obtained as described above.The sonographic visualization of the fetal cerebellum was present as early as 14 to 15 weeks of gestation.The characteristic image of the cerebellum by ultrasonography appears as two lobules on either side of the midline located in posterior cranial fossa. In this study the cerebellum was seen in all examinations,however,before the late third trimester measurements of the transverse cerebellar diameter are easier to perform.

A statistically significant curvilinear relationship was found between the transverse cerebellar diameter and the gestational age $(R^2=0.98;p=0.0001)$,the biparietal diameter$(R^2=0.99;P=0.0001)$,the abdominal circumference$(R^2=0.98;P=0.0001)$,the femur length$(R^2=0.99;0.0001)$,the abdominal circumference $(R^2=0.99;P=0.0001)$ and the head circumference$(R^2=0.98;P=0.0001)$.The pattern of growth of cerebellum measured by the transverse cerebellar diameter follows a second degree polynomial,similar to the growth of biparietal diameter femur length,HC&AC.The equations for the transverse cerebellar diameter against gestational age,BPD,FL,HC and AC are described.

20 pregnant women suspected of IUGRunder went diagnostic ultrasonography.The gestational ages of these pregnancies ranged from 28 to 40 weeks.In all 20 patients in whom the diagnosis of IUGR was made,the TCD correlated with the gestational age as predicted with the last menstrual period and it remained within the normal range of normal for the gestational age.The disparity in gestational age in between the predicted by TCD and that predicted by the remaining biometric parameters was consistently greater than 2.5 weeks that is greater than 2SD above the mean.Additionally the measurements of BPD,AC,FL were well below normal range for the gestational age in most of the cases.

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