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ORIGINAL ARTICLE

Morphological and Morphometric Study of Cerebellum in Human Foetuses

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Abstract:

The cerebellum is a region of the brain which plays an important role in motor control though it does not initiate movement. It contributes for coordination, precision and accurate timing of movement. The cerebellum stands as great modulator of neurologic function and new horizons of cerebellar action were included in neurology and psychiatry. The awareness of cerebellar anatomy has a great neurosurgical importance. A total of 44 apparently normal dead aborted embryos and fetuses of both sexes and of 13 weeks to 36 weeks gestational age were utilized for observing and measuring certain morphological and morphometric parameters of external body and external surface of cerebellum and gestational age related developmental histology of cerebellum. When the results were analyzed it was observed that there is increase in fetal weight with increase in gestational age. Biparietal diameter increased from 13-16 weeks to 29-32 weeks; thereafter it decreased in 33-36 weeks. Head circumference increased with gestational age. Morphological observations of cerebellum are discussed in results. The knowledge of foetal cerebellar anatomy has a tremendous neurosurgical importance and also in the field of forensic medicine.

Keywords: Cerebellum; Morphometry; Vermis; Gestation.

Introduction:

The cerebellum is situated in posterior cranial fossa and it is the major part of hindbrain. Formation of cerebellar hemisphere and vermis are noticed in 12th week and folds of it develop at fourth month.[1] The fetal cerebellum is developing from metencephalon which is the rostral slant of the embryonic hindbrain.[2] Cerebellum has two hemispheres connected by the vermis and it consists of three lobes and two transverse fissures, one horizontal fissure. The primary fissure could be recognized at week 21, and the vermis lobe was visible at week 24.[3]

Cerebellum is one of the first structures in the brain that begins to differentiate but last to mature since its development is spread over a longer period and shows age related changes.[4] Fetal cerebellum measurement is key factors to know the abnormal fetal growth related to central nervous system anomalies, Reece EA.[5] Present study aim is to find out the best parameter suited for estimation of gestational age and quantitative assessment of growth of various parameters in normal fetuses Correlation with the growth cerebellar parameters.

Materials and methods:

The present study on human foetal cerebellum was conducted at department of Anatomy, Sri Venkateswara Medical College, Tirupati, Andhra Pradesh, India by dissection method for observing and recording morphological and morphometric parameters of foetal cerebellum. A total of forty four dead and spontaneously aborted fetuses of both sexes along with relevant obstetric history were collected from the Dept. of Obstetrics and Gynecology after taking consent from the relatives by following the guidelines and permission given by the ethical committee of S.V. Medical College, Tirupati. The Crown-rump and Crown-heel length (Fig. 1) were taken with the foetus stretched to avoid errors in measurements due to the curved position of the foetus.

Preservation of specimen: Subsequently the fetuses were preserved in 10% formalin solution that was injected into the pleura, peritoneum and orbital cavity. The extremities were preserved by multiple injection.

Dissection procedure done for collection of cerebellum: The layers of scalp are removed by making an incision in the midline then the bones of skull cap are removed using the curved scissors for younger fetuses and using saw for removing skull cap of older fetuses. The folds of dura, the falx cerebri and tentorium cerebelli were removed. The attachment of cranial nerves to the base of brain was served close to the foramen from which they exit. The junction of brainstem with spinal cord was separated at the level of foramen magnum. Now, the brain with its coverings was removed from the cranial cavity. Then the cerebellum was lift out from posterior cranial fossa.

Gestational age-wise distribution of aborted fetuses:

A. This group includes study of 44 aborted fetuses, ranging from 13-36 weeks gestational age, in which males fetuse were 18 and female fetuses were 26. All the fetuses included in this group were normal.

B. Total number of fetuses was categorized into 6 gestational age groups according to age wise and sex- wise distribution. 13-16, 17-20, 21-24, 25-28, 29-32 and 33-36 weeks for understanding the morphometry and morphological at close intervals of 4 weeks.

Fetal external morphological and morphometric parameters: gestational age, gender, external appearance, fetal weight, Bi-

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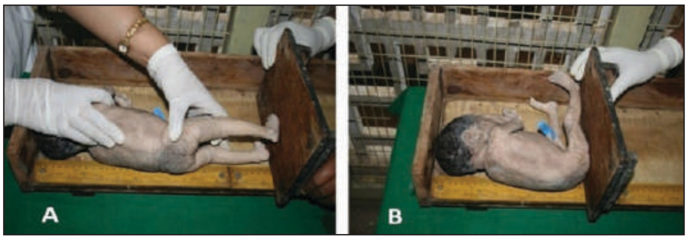

Figure 1. Shows A. Measuring crown-heel length, B. Measuring crown-rump length.

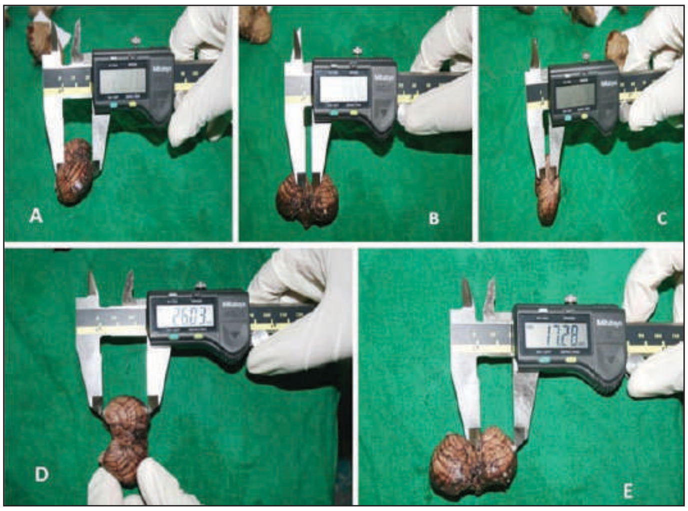

Figure 2. Shows a. Measuring the length of vermis, b. Measuring the width of vermis, c.Measuring the thickness of cerebellum, d. Measuring length of cerebellum, e. Measuring the width of cerebellum.

parietal diameter (B. P. D), head circumference (H.C.), crown-rump length (C.R.L.), crown- heel length (C.H.L.).

Fetal cerebellar external morphological parameters: Morphology of lobes, appearance of primary fissure, postero-lateral fissure and horizontal fissure on the superior and inferior surfaces of both cerebellar hemispheres were observed and recorded in the data sheets according to gestational ages.

Measurements of various cerebellar parameters: The measurements for the both right and left cerebellar hemispheres were taken individually by using paquimeter (Absolute digital verniar calipers) (fig.2).

a). Length of vermis (mm) (fig. 2) - It is measured by paquimeter, placing it along the vermis from anterior cerebellar notch to posterior cerebellar notch.

b). Width of vermis (mm) (fig. 2) - It is measured by keeping the instrument along the width of vermis which was a point located in between the widest part of cerebellar hemispheres.

c). Thickness of vermis (mm) (fig 2) - It is measured by placing the instrument on the vermis at the anterior cerebellar notch.

1. Right lobe - Length (mm) (fig 2) - It is measured at a point where the longest distance was seen for each right cerebellar hemisphere. Width (mm) (fig2) - It is measured at point where the widest width was present. 2. Left lobe - Length (mm) - It is measured at a point where the longest distance was seen for each right cerebellar hemisphere. Width (mm) - It is measured at point where the widest width was present.

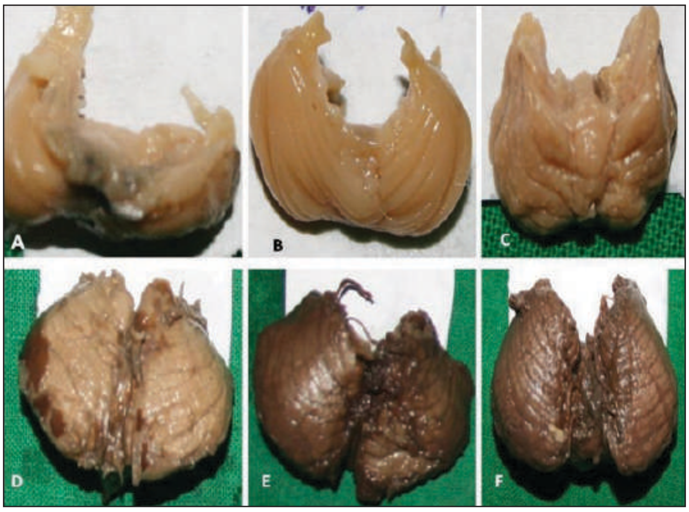

Figure 3. Shows A. 17 weeks, Female- superior surface, B. 13 Weeks, Male- superior surface, C:26 weeks Female inferior surface, C: 22 weeks Male superior surface. D: 30 weeks Male inferior surface E: 36 weeks Male inferior surface.

Statistical analysis: Statistical method has been carried out by using IBM SPSS 20.0 one way ANOVA and correlation analysis of variance technique applied at 5 % level of significance.

Results:

A total of 44 apparently normal dead and aborted embryos and fetuses of both sexes and of 13 weeks to 36 weeks gestational age were utilized for observing and measuring certain morphological and morphometric parameters of external body and external surface of cerebellum and also histological features of cerebellum. The results of the present study were described in the following order.

External foetal morphology: All the fetuses observed in this group were apparently normal.

External foetal parameters/morphometry: The external body parameters of foetal weight (FW), crown- rump length (CRL), crown- heel length (CHL), head circumference (HC) and Bi-parietal diameter (BPD) were statistically analyzed by calculating independent mean, standard deviation and sample t test for each gender and represented in table 5.2. The foetal weight was measured in grams. Other morphometric parameters were measured in centimeters.

Table 1 Showing the one way ANOVA for various external body parameters in the sample studied in 4 week- wise gestational age groups of aborted fetuses. This table reveals that by carrying out ANOVA, Foetal weight increased significantly in all groups. CRL increased with significant values. CHL decreased in 17-20 and 21-24 weeks and increased in 13-16, 25-28, 29-32 and 33-36 weeks groups with significant values. BPD decreased in 17-20 weeks and 33-36 weeks of gestational age, it is increased with significant value in remaining age groups. HC increased significantly in all age groups. Table 2 is showing the one way ANOVA by age for various external parameters of cerebellum in the sample studied in week-wise gestational age groups of aborted fetuses. This table reveals that by carrying out ANOVA, vermis length decreased in 25-28 weeks and remaining

Table 1. Showing, mean, standard error, one way anova and significance levels for external body parameters in aborted fetuses of different gestational age groups.

Para-meters	13-16 weeks		17-20 weeks		21-24 weeks		25-28 weeks		29-32 weeks		33-36 weeks		F-value	Sig.
	Mean	S.E	Mean	S.E	Mean	S.E	Mean	S.E	Mean	S.E	Mean	S.E		
Weight	105.00	45.00	473.33	93.23	685.56	73.41	871.82	127.37	1521.50	191.11	2125.00	186.53	17.165	0.000*
C RL	11.75	1.75	15.75	0.51	21.14	0.52	23.67	0.77	28.14	0.61	33.88	0.45	87.092	0.000*
C HL	32.75	11.25	23.50	0.85	32.37	1.30	36.89	1.43	43.14	0.98	51.27	2.49	41.439	0.000*
BPD	8.10	0.10	6.78	0.33	8.23	0.62	8.90	0.62	10.60	0.66	9.65	1.06	3.984	0.009*
HC	12.50	1.50	15.08	0.78	22.63	0.95	24.28	0.94	27.01	2.08	32.87	0.61	16.679	0.000*

Table 2. Showing, mean, standard error, one way anova and significance levels for cerebellar parameters in different gestational age groups.

Parameters	13-16 weeks		17-20 weeks		21-24 weeks		25-28 weeks		29-32 weeks		33-36 weeks		F-value	Sig.
	Mean	S.E	Mean	S.E	Mean	S.E	Mean	S.E	Mean	S.E	Mean	S.E		
Vermis length	4.14	0.50	5.63	0.74	10.14	1.43	9.97	1.08	12.62	1.01	17.11	0.76	10.169	0.000*
Vermis width	2.71	0.87	3.40	0.50	4.37	0.22	3.74	0.37	5.29	0.45	4.26	0.29	3.566	0.015*
Vermis thickness	1.48	0.38	3.30	0.31	3.66	0.28	2.93	0.41	3.92	0.33	3.42	0.39	1.280	0.295NS
RL length	6.66	1.18	7.98	0.89	13.21	1.16	15.45	1.45	18.98	1.63	26.60	1.31	17.549	0.000*
RL width	5.08	0.82	6.03	0.56	11.30	1.34	12.16	1.32	15.57	1.46	19.91	0.46	11.866	0.000*
LL length	6.66	1.18	7.52	0.74	12.74	1.26	15.29	1.57	18.64	1.53	26.19	1.04	17.543	0.000*
LL width	5.42	0.49	6.25	0.49	10.85	1.04	22.00	10.20	14.90	1.46	20.04	0.62	1.024	0.408NS
Cerebellum weight	0.35	0.15	0.58	0.15	2.40	0.52	4.76	1.28	7.44	1.15	14.53	1.93	16.461	0.000*

Table 3. Showing, correlation analysis between foetal cerebellar morphometry and external foetal morphometry.

Correlation values between Foetal and Cerebellar Parameters		Foetal Parameters			
		C R	C H	BPD	HC
Cerebellar Parameters	Vermis length	0.779	0.652	0.392	0.627
	Vermis width	0.394	0.181	0.497	0.292
	Vermis thickness	0.250	0.026	0.357	0.177
	RL length	0.858	0.707	0.460	0.655
	RL width	0.820	0.710	0.375	0.658
	LL length	0.860	0.713	0.446	0.660
	LL width	0.279	0.217	0.170	0.277
	cerebellum weight	0.803	0.749	0.249	0.613

gestational age groups it increased with significant value. Vermis width decreased in 25-28, 33-36 weeks and remaining age groups increased significantly. Vermis thickness is decreased in 25-28, 33-36 groups, and increases in remaining age groups but it is statistically not significant. Right lobe length and width, left lobe length increased significantly in all gestational age groups. Left lobe width decreased in 29-32 group and in remaining age groups width is increased but it is statistically not significant. Cerebellum weight is increased significantly in all gestational age groups.

Table 3 shows the correlation values between the foetal and cerebellar parameters. The bold values represent significant correlations which were tested at 5% level of significance. All the parameters are positively correlated and the parameters vermis length is highly correlated with CR, CH and HC. Similarly, the parameters RL length, RL width, LL length and cerebellum weight are highly correlated with CR, CH and HC. The rest of the parameters are not significantly correlated.

Morphological observations of cerebellum: Observations in group-a (13-16 wks): External surface of cerebellum is smooth. Vermis and lobes of cerebellum could not be clearly demarcated (Fig.3). The right and left lobes are symmetrical, and fissures are lightly demarcated.

Observations in group-b (17-20 wks): Beginning of formation of folia were observed. Early stage of demarcation of Vermis and lobes of cerebellum observed (Fig.3). The right and left lobes are symmetrical, and fissure on hemispheres are clearly seen.

Observations in group-c (21-24 wks): Folia could be demarcated. Vermis and lobes of cerebellum clearly demarcated than previous gestation age group (Fig.3). The right and left lobes are symmetrical, and fissure on hemispheres are clearly demarcated.

Observations in group-d (25-28 wks): Folia could be clearly demarcated. Vermis and lobes of cerebellum well demarcated (Fig.3). The right and left lobes are symmetrical, and fissures on hemispheres well demarcated.

Observations in group-e (29-32 wks): Folia could be well demarcated. Vermis and lobes of cerebellum well demarcated. The right and left lobes are symmetrical, and fissures on hemispheres are well demarcated (Fig.3).

Observations in group-f (33-36 wks): Folia could be clearly demarcated. Vermis and lobes of cerebellum well demarcated. The right and left lobes are symmetrical, and fissures on hemispheres are well demarcated than other previous age groups (Fig.3).

Discussion:

When the results were analyzed it was observed that there is increase in fetal weight with increase in gestational age. Biparietal diameter increased from 13-16 weeks to 29-32 weeks; thereafter it decreased in 33-36 weeks. Head circumference increased with gestational age.

The formation of folia was gradually increased from 20-30 weeks of gestational age.[6-8] but it was not mentioned in the literature when it will start forming. According to Parisi et al., [9] by 4 months gestation, the vermis becomes fully foliated. In the present study the earliest age of the specimen is that of 13 weeks in which folia were not observed and in 17 weeks specimen the folia were observed. Based on the observations in the present study it can be concluded that they start appearing between 13 and 17 weeks.

According to Liu F et al.,[10] primary fissure was the first to be visualized and was detectable as early as 14^{th} week. In the present study it appeared at 13 weeks and is earlier than reported in literature by Fei Liu et al. and delayed by one week when compared with the report, it appears sometimes during 12^{th}

week.[11] According to Sir Arthur Keith[12] at the end of the 4th month four fissures are seen in human cerebellum. The posterolateral fissure could be recognized at 17th week as stated in the literature by Fei Liu et al. but in the present study it appeared as early as 13 weeks.

Based on MRI studies[13] and based on ultrasonographic studies[14] reported that at around 11 to 12 weeks, the cerebellum and early vermis can be noticed along the cranial aspect of the fourth ventricle. By 13 to 14 weeks, the early fastigial point can be seen developing as a crease along the ventral surface of the cerebellar plate. In the present study at 13 weeks vermis and cerebellar hemispheres could be identified but they cannot be demarcated clearly. At 17 weeks the vermis and lobes could be clearly demarcated. The size of the cerebellum (or) transverse cerebellar diameter (TCD) is useful biometric parameter to estimate gestational age in the second trimester.[15] The ratio between TCD and vermis length and between TCD and vermis width decreases with gestational age. These results show trajectory development in MRI. These parameters increase our understanding of normal cerebellar development in fetus, and facilitate the diagnosis of pathological intrauterine changes. All the parameters of vermis presented significance with gestational age group except thickness of vermis. The length of both lobes and width of Right lobe were significant with gestational age groups. Cerebellum weight is increased significantly in all gestational age groups.

All the foetal and cerebellar parameters are positively correlated and vermis length is highly correlated with CRL, CHL and HC. Similarly, the parameters RL length, RL Width, LL Length and cerebellum weight are highly correlated with CRL, CHL and HC. The rest of the parameters are not significantly correlated. Occlusion: All the external foetal morphometric parameters are significant with increased gestational age. In the present study all the fissures appeared earlier than that reported in the literature. The external parameters of cerebellum and foetal external parameters are positively correlated. All the parameters of cerebellum except thickness of vermis and left lobe width presented significance with gestational age.

The information of cerebellar anatomy has got incredible importance in neurosurgical practice. Future studies might engage assessment of the cerebellum at other gestational ages of foetuses. The purpose of this study is to use the results to estimate the cerebellum in fetuses with malformations of the CNS also. While present method is difficult to be used in vivo evaluation, it can contribute an anatomical foundation for the diagnosis of foetal neuro abnormalities. The normal parameters and dimensions of the vermis in different gestational periods are tremendously important in evaluating the posterior cranial fossa abnormalities because vermian defect are the main features of occurrence of neural defects and malformations.

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