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Research Article

Evaluation of Cerebral Hemisphere and Ventricular Development in the Fetal Period Using Magnetic Resonance Imaging

Fetal Dönemde Beyin Hemisferleri ve Ventrikül Gelişiminin Manyetik Rezonans Görüntüleme ile Değerlendirilmesi

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Abstract
Monitoring fetal brain development is of great importance for the early diagnosis and management of anomalies. Magnetic Resonance Imaging, which is used for this purpose, allows for detailed morphometric analyses of structures such as the cerebral hemispheres and the ventricular system. For this purpose, it was planned to evaluate the development of the brain hemispheres and lateral ventricles throughout the fetal period and to obtain morphometric data. The study was conducted on 120 deceased human fetuses (63 males, 57 females) with gestational ages ranging from 12 to 40 weeks, who had no external pathology or anomalies. Initially, general external parameters were measured to determine the age of the fetuses. Then, using Magnetic Resonance Imaging, images of the cranial region were obtained in sagittal, axial, and coronal planes. From these images, two-dimensional parameters of the brain hemispheres and lateral ventricles, as well as volumetric parameters of the brain hemispheres, were evaluated. The mean and standard deviations of the obtained parameters were determined according to gestational weeks and trimester groups. There was no statistically significant difference in any of the parameters between the right and left sides or between genders ($p>0.05$). A positive correlation was found between all the obtained parameters and gestational age. We believe that the data obtained throughout the study will be helpful in evaluating the development of the cerebral hemispheres and lateral ventricles in disciplines such as obstetrics, perinatology, and pediatrics, in earlier detection of regional anomalies, and in determining treatment possibilities.
Keywords: Brain Hemisphere, Fetal Development, Human Fetus, Intracranial Nerve System, Lateral Ventricle.

Özet
Fetal beyin gelişiminin izlenmesi, anomalilerin erken tanı ve yönetimi açısından büyük önem taşımaktadır. Bu amaçla kullanılan manyetik rezonans görüntüleme, serebral hemisferler ve ventriküler sistem gibi yapılar üzerinde detaylı morfometrik analizler yapılmasına olanak tanımaktadır. Bu amaçla fetal dönem boyunca beyin hemisferleri ve lateral ventrikül gelişimini değerlendirmek ve morfometrik bilgiler elde edilmesi planlandı. Çalışma, yasları 12-40 gebelik haftası yaşı arasında değişen, eksternal patolojisi ve anomalisi olmayan, 120 adet ölü insan fetusu (63 males, 57 females) üzerinde gerçeklestirildi. İlk olarak fetusların yaşının belirlenmesi için genel eksternal parametreler ölçüldü. Ardından Magnetic Rezonans Görüntüleme yöntemi kullanılarak kranium bölgesinin sagittal, aksiyal ve coronal eksenlerde görüntüleri alındı. Alınan görüntülerden beyin hemisferleri ve lateral ventriküllere ait 2 boyutlu parametreler ile beyin hemisferlerine ait hacim parametreleri değerlendirildi. Alınan parametrelerin gestasyonel hafta ve trimester gruplara göre ortalama ve standart sapmaları belirlendi. Bütün parametrelerde sağ ve sol taraflar arası karşılaştırmasında veya cinsiyetler arasında anlamlı fark yoktu ($p>0.05$). Alınan bütün parametreler ile gestasyonel yas arasında pozitif korelasyon bulundu. Çalışma boyunca elde edilen verilerin kadın doğum, perinatoloji ve pediatri gibi bilim dallarında beyin hemisferleri ve lateral ventriküllerinin gelişimini değerlendirmede, bölge anomalilerinin daha erken saptamasında ve tedavi olanaklarının belirlenebilmesinde yardımcı olacağını düşünmekteyiz.
Anahtar Kelimeler: Beyin Hemisferleri, Fetal Gelişim, İnsan Fetusu, İntrakranial Sinir Sistemi, Lateral Ventrikül.

Introduction

The fetal period is a critical developmental phase lasting from the 9th week of pregnancy until birth, during which body growth accelerates and organs mature. During this period, especially in the second trimester, the fetal brain and central nervous system (CNS) exhibit significant morphological changes. However, due to its complex anatomical structure and the limited ability of transabdominal ultrasonography (USG) to provide detailed imaging, the fetal brain is one of the most challenging organs to assess during the prenatal period (1) . As a result, the risk of overlooking rare anomalies increases (2,3). Yet, accurately identifying brain development is essential, as it has significant implications for health in later stages of life (4).

The early diagnosis of CNS anomalies is possible through a detailed understanding of normal CNS development. However, morphometric data on the development of the fetal CNS remain limited in the literature. Most existing studies are based on in vivo methods and generally focus on a specific gestational period or anatomical structure (5–9). In particular, comprehensive trimester-based comparisons of the proportional growth dynamics of structures such as the cerebral hemispheres and lateral ventricles are insufficient (10–12). The main reason for this is the inability to clearly visualize fetal structures with USG and MRI (2,3).

USG is the primary choice in prenatal imaging to avoid the teratogenic and carcinogenic effects of radiation. Despite the fact that recent technological advances have enabled USG to provide three-dimensional image processing, its use is still considered limited (13). Therefore, in cases where USG is insufficient and from the mid-trimester onward, magnetic resonance imaging (MRI) plays a significant role in providing additional information (14). MRI is suitable for examining the developing fetal brain due to its lack of ionizing radiation, high soft tissue contrast, and being a minimally invasive method (4,14). Especially in high-risk pregnancies, MRI makes important contributions to the accuracy of prenatal diagnosis (15–17). However, starting from the 10th gestational week, increasing fetal movements reduce MRI image quality and make evaluation more difficult (18).

This study aimed to morphometrically evaluate the development of fetal brain hemispheres and lateral ventricles using MRI over a wide gestational age range with deceased fetal materials. In this way, a more comprehensive description of the development of the brain hemispheres and lateral ventricles during the fetal period would be achieved, and guiding data would be provided for diagnostic processes based on USG and MRI. The findings obtained are expected to contribute to the evaluation of CNS development and the early detection of possible anomalies in the fields of obstetrics and gynecology, perinatology, and pediatrics.

Material and Method

An a priori power analysis based on two independent samples was conducted using the G*Power software. Assuming a medium effect size (Cohen's $d = 0.5$) and a target power of 0.80 with $\alpha = 0.05$, the analysis indicated that a minimum of $n = 64$ hemispheres per group (right and left) - a total of $n = 128$ hemispheres - would be required. In our study, a total of $n = 240$ hemispheres were included, consisting of $n = 120$ right and $n = 120$ left (independent) hemispheres.

The study was conducted on human fetal cadavers (63 males, 57 females), aged between 12 and 40 gestational weeks, which were obtained with the consent of their families from Isparta Maternity and Children's Hospital between 1996 and 2009, and collected in the Laboratory of the Department of Anatomy at the Faculty of Medicine, Suleyman Demirel University. The causes of death of the fetal cadavers were unknown. Fetuses with anomalies or cranial deformities were excluded from the study. In addition, 11 fetuses with intracranial hemorrhage detected by MRI were not included in the study. All fetuses were preserved in a 10% formaldehyde solution. According to previous studies, formaldehyde is known to cause approximately 3% shrinkage in tissues. Therefore, this shrinkage rate should be taken into account when evaluating the data (19). Furthermore, approval for the study was obtained from the relevant official institutions and the Ethics Committee of the Faculty of Medicine at Suleyman Demirel University prior to the study (Date: 13/12/2000, Decision No: 1).

To determine gestational age, crown-rump length (CRL), biparietal diameter (BPD), head circumference (HC), femur length (FL), and foot length (FtL) were used as criteria (20).

Fetuses were also examined by trimester in four groups: (21,22)

- 1st trimester (8-12 weeks): 2 females
- 2nd trimester (13-25 weeks): 23 males, 29 females

- 3rd trimester (26-37 weeks): 25 males, 23 females
- Full-term (38-40 weeks): 13 males, 3 females

Parameters taken from MRI sections

The imaging of the fetal cranium was performed using a 0.2 Tesla GE (General Electric) MRI device located at the Department of Radiodiagnostics, Suleyman Demirel University. All imaging was carried out in three planes using a knee coil: *Sagittal plane*: T1-weighted images (TR: 300, TE: 17), FOV: 200 mm, section thickness: 5 mm, spacing: 0 mm, matrix: 128×256, *Coronal plane:* T2-weighted FSE (Fast Spin Echo) images (TR: 3250, TE: 117), FOV: 200 mm, section thickness: 6 mm, spacing: 0 mm, matrix: 128×192, *Transverse plane:* T2-weighted FSE images (TR: 4300, TE: 117), FOV: 200 mm, section thickness: 4.5 mm, spacing: 0 mm, matrix: 128×224.

All acquired images were transferred to CD format, and the programs EnlilPACS CD viewer and ClearCanvas Workstation were used for evaluation. Morphometric measurements were taken from the two-dimensional images in the three planes. The measured parameters are listed below:

Morphometric measurements of cerebral hemispheres:

Cerebral Hemisphere Width: In the transverse plane, this is the total distance between the sagittal axes passing through the lateral boundaries of both cerebral hemispheres at the widest section (Figure 1).

Anterior-Mid Hemisphere Width: In the widest section of the transverse plane, this is the transverse distance measured through a plane passing the midpoint of the anterior half of the cerebral hemisphere width (Figure 1).

Posterior-Mid Hemisphere Width: In the widest section of the transverse plane, this is the transverse distance measured through a plane passing the midpoint of the posterior half of the cerebral hemisphere width (Figure 1).

Cerebral Hemisphere Height: In the widest section of the coronal plane, this is the vertical distance between the inferior and superior boundaries of the right and left cerebral hemispheres (Figure 2).

Cerebral Hemisphere Depth: In the longest section of the transverse plane, this is the sagittal distance between the anterior and posterior boundaries of the hemispheres (Figure 3).

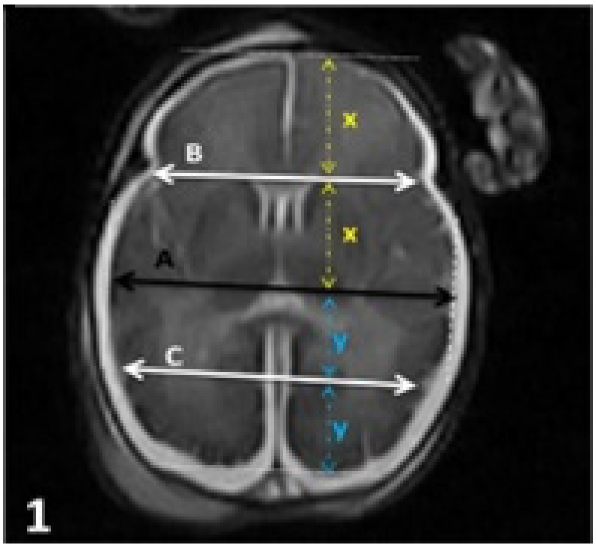

Figure 1. 39 weeks of gestation age. axial cranium MR image obtained with T2-weighted sequence in a male fetus. **A.** right and left cerebrum hemisphere width. **B.** Anterior-middle width of the brain hemisphere. **C.** Posterior-middle width of the brain hemisphere.

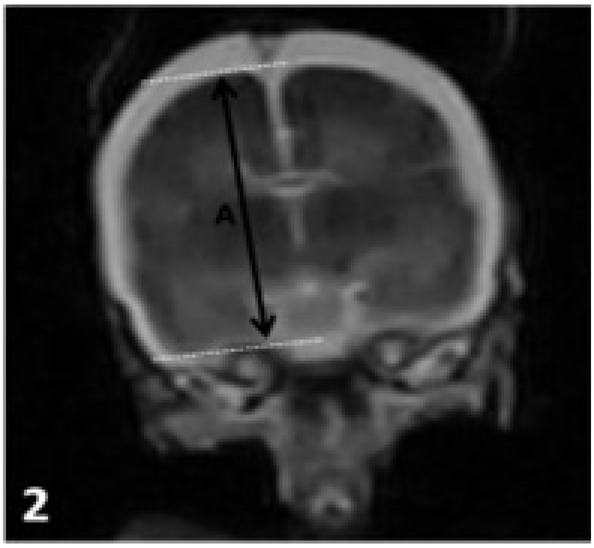

Figure 2. 27 weeks of gestation age. coronal cranium MR image obtained with T2-weighted sequence in a male fetus. **A.** Right hemispherium cerebri height.

The following measurements related to the lateral ventricles were evaluated separately for the right and left sides:

Lateral ventricle depth (right/left): In the transverse plane, the sagittal distance between the anterior and posterior horns was measured at the section where the lateral ventricles appeared the longest (Figure 5).

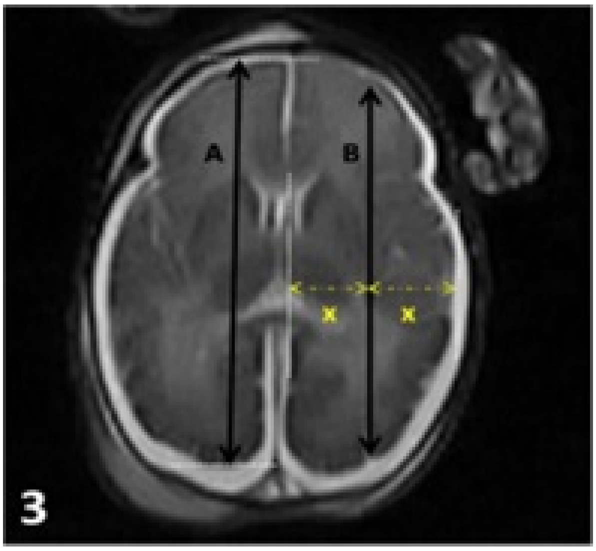

Figure 3. 39 weeks of gestational age. axial cranial MR image obtained with T2-weighted sequence in a male fetus **A.** Right hemispherium cerebri depth. **B.** Mid-depth of the left hemispherium cerebri.

Volume parameters:

The volume of the cerebral hemispheres was calculated based on the stereological Cavalieri principle (23). In this method, the areas of the right and left hemispherium cerebri were measured on transverse MRI slices using the ClearCanvas Workstation software (Figure 4).

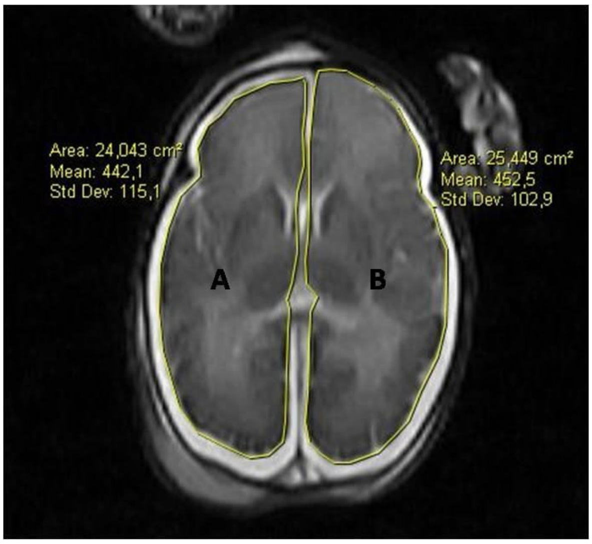

Figure 4. 39 weeks of gestation age. transverse cranial MR image of a male fetus. **A.** Right hemispherium cerebri areas calculated by outlining the boundaries of the right hemispherium. **B.** Left hemispherium cerebri area calculated by outlining the boundaries of the left hemispherium.

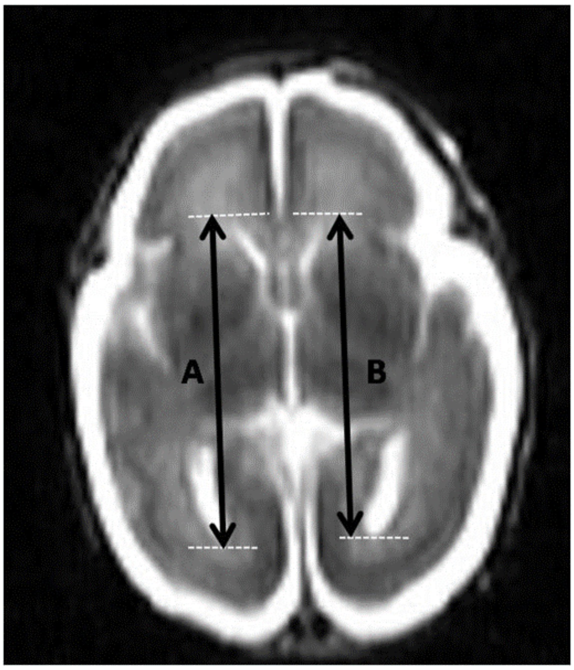

Figure 5. 27 weeks of gestation age. transverse cranial MR image of a male fetus. **A**. right lateral ventricle depth. **B**. Left lateral ventricle depth.

Statistical Evaluation

All statistical analyses were performed using the SPSS v15.0 software (SPSS Inc., 2007). The means and standard deviations of all parameters obtained according to sex, gestational age, and groups were calculated. One-way analysis of variance (ANOVA) was used for comparisons between groups. In multiple comparisons for ANOVA, the significance level was re-evaluated using the Bonferroni correction. The relationships between gestational age and morphometric parameters were examined using Pearson's correlation test. For comparisons between sexes and sides, independent samples t-test or Mann-Whitney U test was applied. A $p<0.05$ was considered statistically significant.

Results

In the assessments conducted on 120 fetuses (63 males, 57 females) included in this study, fundamental biometric parameters such as crown-rump length (CRL), head circumference (HC), biparietal diameter (BPD), femur length (FL), and foot length (FtL) were determined (Table 1). Based on these parameters, the fetuses were categorized into weekly and trimester groups. No statistically significant difference was observed between the sexes in terms of general parameters ($p>0.05$, Table 1).

Table 1. Mean values of general fetal parameters obtained throughout the fetal period according to gestational weeks (mm).

Gestational age (week)	n	Head circumference (HC)	Biparietal diameter (BPD)	Crown-rump length (CRL)	Femur length (FL)	Foot length (FtL)
12	2	88	22	91	20	13
13	3	98	25	98	24	16
14	4	105	29	104	29	17
15	4	116	32	107	30	18
16	5	117	33	116	30	20
17	4	130	36	123	34	21
18	4	147	41	147	38	27
19	4	150	43	148	41	28
20	4	168	48	156	43	30
21	4	185	48	166	49	35
22	4	200	56	186	49	36
23	4	208	56	186	53	39
24	5	218	58	194	59	42
25	5	228	59	203	62	43
26	6	228	60	211	62	44
27	4	248	64	229	65	53
28	5	265	65	238	69	54
29	3	270	68	241	73	55
30	6	277	71	252	74	55
31	4	281	74	263	75	59
32	3	296	77	266	80	61
33	4	297	77	270	81	63
34	2	305	79	278	84	65
35	3	306	79	285	85	68
36	5	322	80	291	88	72
37	3	333	93	292	90	72
38	5	349	93	292	96	74
39	3	353	96	312	99	77
40	8	365	96	326	100	78

Morphometric measurements of the cerebral hemispheres

Based on the data obtained, measurements of cerebral hemisphere height, total width of the cerebral hemispheres, anterior-mid width, posterior-mid width, and cerebral hemisphere depth were evaluated according to gestational week (Table 2) and trimester (Table 3).

The means and standard deviations of these measurements by trimester groups are presented in Table 3. For the measurements of height and depth, the right and left hemispheres were evaluated separately; however, since no significant difference was found between the sides, the table presents the mean values of the right and left hemispheres.

All dimensional parameters obtained were found to increase significantly with gestational age, and this increase was statistically significant (Table 2). In comparisons between trimesters, a significant difference was observed among the groups for all parameters ($p<0.05$, Table 3).

Volume of cerebral hemispheres

Volume measurements calculated using the ClearCanvas Workstation program based on the principle of the stereological Cavalieri method showed a significant increase with gestational age (Tables 4). No difference was found between the volumes of the right and left hemispheres ($p>0.05$). However, comparisons between months and between trimesters ($p<0.05$, Table 3) revealed significant differences among all groups.

Lateral ventricle parameters

Depth measurements obtained from the right and left lateral ventricles were analyzed at the levels of gestational weeks (Table 4) and trimesters (Table 3). A significant positive correlation was found between lateral ventricle depths and gestational age ($p<0.001$). No difference in depth was observed between the right and left sides ($p>0.05$). In trimester comparisons, a significant difference was found among all groups except between the 1st and 2nd trimesters ($p<0.05$, Table 3).

Discussion

This study presents a comprehensive analysis examining the morphometric development of the cerebral hemispheres and lateral ventricles, which constitute the majority of the central nervous system during the fetal period. The data obtained demonstrate that both the dimensional changes of the cerebral hemispheres and lateral ventricles, as well as the volumetric changes of the cerebral hemispheres, significantly increase with gestational age. Cerebral hemisphere volumes also quantitatively support this growth dynamic. Furthermore, statistically significant differences were observed in many parameters when comparing trimester groups. These findings suggest that they may aid in the imaging and evaluation of neuroanatomical development during the fetal period and fetal development during the prenatal period in clinical practice.

Documenting morphometric data in the early fetal period is important for evaluating normal growth. Such data can provide precise information about brain structures and may contribute to the early diagnosis of brain injuries. Nevertheless, it is not possible to directly intervene with a normal fetus in utero, and USG is generally preferred during routine check-ups. Therefore, in most studies, USG data are more commonly available than MRI data. In MRI studies, however, due to differences such as the use of live or deceased fetal material, limited gestational weeks (24–26), differences in the placement of anatomical measurement points (24), and the fact that average values in studies are generally not presented in table format (24,25), direct comparisons are not always possible. For these reasons, Jarvis et al. (18) stated that the data obtained cannot be directly compared with other MRI data. Similarly, in this study, comparisons could only be made based on the data that were accessible.

Evaluation of morphometric measurements of cerebral hemispheres

In this study, it was found that the width, depth, mid-depth, and height measurements of the right and left cerebral hemispheres increased significantly with gestational age. This indicates that hemispheric growth continues dynamically during the fetal period.

Table 2. Mean values of hemispheric parameters obtained throughout the fetal period according to gestational weeks (mm).

Gestational age (week)	n	Cerebral Hemisphere Height	Cerebral Hemisphere Width			Cerebral Hemisphere Depth
			Total Hemisphere Width	Anterior-Mid Hemisphere Width	Posterior-Mid Hemisphere Width	
12	2	17	18	14	16	25
13	3	20	23	15	18	27
14	4	20	23	15	20	28
15	4	21	24	16	21	30
16	5	21	24	17	22	32
17	4	23	25	18	22	35
18	4	25	30	21	27	37
19	4	27	32	21	28	38
20	4	30	32	23	28	43
21	4	31	36	25	31	46
22	4	37	41	26	33	54
23	4	38	41	32	35	56
24	5	39	44	33	37	59
25	5	40	46	34	41	60
26	6	42	48	39	44	63
27	4	48	51	40	44	70
28	5	48	53	45	49	74
29	3	50	56	46	49	75
30	6	51	57	47	51	77
31	4	52	61	48	53	78
32	3	53	61	48	55	79
33	4	54	61	49	56	80
34	2	55	62	50	56	86
35	3	59	64	51	57	87
36	5	60	65	52	57	88
37	3	61	66	55	57	89
38	5	63	71	55	62	90
39	3	66	73	56	62	93
40	8	67	76	62	66	95

The average of right and left measurements is presented.

Table 3. Morphometric measurements of brain hemispheres, volumes, and ventricular depths by trimester groups (Mean ± SD).

	1st trimester (9–12 weeks) a	**2nd trimester (13–25 weeks) b**	**3rd trimester (26–37 weeks) c**	**Full-term (38–40 weeks) d**	**Total (9–40 weeks)**	**p value**
n	2	55	47	16	120	-
Cerebral hemisphere height (mm)	17.25±0.64	29.71±9.05	52.38±8.69	65.58±4.78	43.16±16.29	^{ab} p=*0.018* ^{bc} p<*0.001* ^{cd} p<*0.001*
Total hemisphere width (mm)	18.00±0.28	33.34±9.33	57.85±9.00	73.77±5.52	48.07±17.79	^{ab} p=*0.017* ^{bc} p<*0.001* ^{cd} p<*0.001*
Anterior-mid hemisphere width (mm)	14.60±0.71	23.72±8.81	46.49±8.58	58.96±5.60	37.19±16.06	^{ab} p=*0.037* ^{bc} p<*0.001* ^{cd} p<*0.001*
Posterior-mid hemisphere width (mm)	16.15±0.92	28.72±9.74	51.48±8.09	64.21±4.94	42.16±16.31	^{ab} p=*0.037* ^{bc} p<*0.001* ^{cd} p<*0.001*
Cerebral hemisphere depth (mm)	24.65±1.06	42.58±13.15	77.48±12.11	90.45±22.01	62.33±24.44	^{ab} p=*0.019* ^{bc} p<*0.001* ^{cd} p<*0.001*
Right cerebral hemisphere volume (mm³)	2358.90 ± 136.83	15772.75 ± 12325.60	69564.54 ± 27735.19	140020.77 ± 38394.98	53184.04 ± 48602.92	^{ab} p=*0.019* ^{bc} p<*0.001* ^{cd} p<*0.001*
Left cerebral hemisphere volume (mm³)	2263.95 ± 89.73	15652.86 ± 2127.42	69767.49 ± 27851.05	133685.42 ± 21147.85	52362.29 ± 45791.08	^{ab} p=*0.017* ^{bc} p<*0.001* ^{cd} p<*0.001*
Right lateral ventricle depth (mm)	22.70 ± 1.84	31.89 ± 8.44	50.23 ± 7.56	54.34 ± 7.41	41.92 ± 12.73	^{ab} p=*0.113* ^{bc} p<*0.001* ^{cd} p<*0.001*
Left lateral ventricle depth (mm)	22.25 ± 2.19	32.53 ± 8.53	50.85 ± 7.13	55.74 ± 8.38	42.63 ± 12.87	^{ab} *p=0.08* ^{bc} p<*0.001* ^{cd} p=*0.21*

P<0.05; intergroup differences in all parameters

When the width, anterior-mid width, posterior-mid width, height, and depth measurements obtained from the cerebral hemispheres were evaluated, a significant difference was observed between the trimester groups. Due to the three-dimensional structure of the brain, the ratios between the measured parameters were also evaluated and compared across groups. In this context, the mean values of the width/depth, width/height, and height/depth ratios of the cerebral hemispheres were calculated and analyzed among the trimester groups using one-way ANOVA. The findings revealed that these ratios did not show a statistically significant difference between the trimester groups. This result indicates that the cerebral hemispheres exhibit proportional growth in width, depth, and height dimensions during the fetal period.

In the comparison of the anterior-mid width and posterior-mid width parameters of the cerebral hemispheres, a difference was found, with the posterior-mid width being greater (p < 0.001, Table 3). However, when the ratio between the anterior-mid and posterior-mid width parameters was examined, there was no difference among the trimester groups. These results show that the posterior part of the cerebral hemispheres is wider throughout the entire fetal period and that both the anterior and posterior parts grow by expanding at the same rate during the fetal period.

Evaluation of Cerebral Hemisphere Volume Measurements

When cerebral hemisphere volumes were evaluated in terms of side and gender, no significant difference was found. The findings indicate that the right and left hemispheres grow symmetrically and proportionally throughout fetal development.

In a study conducted by Roelfsema et al. (27) using a three-dimensional sonographic method, a linear increase in cerebral volume with gestational age was also reported. The same study noted a discrepancy between the volume values obtained through sonographic measurements and those from postmortem fetuses; this difference was attributed to factors such as postmortem brain tissue dehydration, cause of death, and vascular or inflammatory pathologies.

Table 4. Mean values of right and left cerebrum hemisphere volume (mm³) and anterior-posterior depth of the lateral ventricle (mm) obtained throughout the fetal period according to gestational weeks.

Gestational age (week)	N	Right cerebral hemisphere volume (mm³)	Left cerebral hemisphere volume (mm³)	Right lateral ventricle depth (mm)	Left lateral ventricle depth (mm)
12	2	2359	2264	22	22
13	3	3597	3475	23	22
14	4	4314	4232	23	23
15	4	4404	4386	25	25
16	5	4596	4619	25	25
17	4	6509	6730	26	26
18	4	8419	8625	27	28
19	4	10099	9372	31	31
20	4	13865	14072	32	33
21	4	17924	18004	34	34
22	4	25343	24820	39	41
23	4	27384	26853	41	41
24	5	31269	30778	41	42
25	5	32702	32657	42	44
26	6	34315	34476	45	44
27	4	44450	46036	46	46
28	5	58387	56225	47	48
29	3	63425	65844	47	48
30	6	64970	69758	48	48
31	4	71095	72551	48	49
32	3	75795	74883	49	51
33	4	76924	79303	49	51
34	2	87936	86532	54	54
35	3	96162	93743	55	55
36	5	96858	95091	55	56
37	3	98832	96802	56	57
38	5	122002	120591	57	57
39	3	138514	139058	57	58
40	8	151847	139855	58	58

The average of right and left measurements is presented.

In the study by Gong et al., it was reported that between the 27th and 40th gestational weeks, brain volume ranged from 121.5 to 371.2 mL, with an average volume of 255.4 ± 65.0 mL, and that brain volume increased by an average of 2.3 mL per day throughout the third trimester (23). These findings are also consistent with the results of our study. In addition, there are studies that have calculated total brain volume. Accordingly, Gholipour et al. (26) reported the average total brain volume at 25 weeks as 90 mL, while Clouchoux et al. (25) stated it as 85 mL and emphasized that it increases with gestational age (25,26). Rajagopalan et al. (28) found the total brain volume in fetuses in the second trimester to be 88 mL at 25 weeks and 120 mL at 28 weeks. When all these studies are evaluated, it becomes apparent that volumes were measured using different reference points in fetal brain structures. It is therefore considered that determining standard, applicable measurement techniques for fetal brain measurements would be beneficial for making reliable comparisons. Consequently, it was suggested that rather than presenting results as volumes, evaluating and interpreting the ratios of the structures to each other could eliminate differences between methods.

In this study, growth rates of brain hemisphere volumes were also evaluated, and an approximately 6-fold increase was observed between the 1st and 2nd trimesters, a 4.5-fold increase between the 2nd and 3rd trimesters, and an approximately 2-fold increase between the 3rd and 4th trimesters (Table 3). The decrease in this fold-change between trimesters can be explained by the slowing of volumetric growth rate due to the deepening of gyri and sulci in the later weeks of the fetal period.

What distinguishes our study from previous ones is that volume data were obtained using MRI imaging in postmortem fetal samples without anomalies and with a wider gestational age range. In previous research, measurements of CNS structures were mostly limited to specific weeks or included a higher proportion of anomalous foetuses (25). However, a detailed volumetric analysis of central nervous system structures during the fetal period facilitates the interpretation of prenatal imaging methods (especially ultrasonography) and helps establish normative reference data.

In clinical practice, skull measurements are most commonly used to assess brain size, and linear measurements of brain tissue are not routinely performed. However, this approach has limitations in terms of reliability, as skull size does not solely depend on brain development but can also vary due to pathological conditions such as fetal hydrocephalus (29) Therefore, it is important to develop methods that allow for accurate and reproducible measurement of intracranial structure volumes. We believe that the data obtained in this study may contribute to a wide range of applications, from routine pregnancy screenings to the identification of fetal neuropathologies (18).

Evaluation of Lateral Ventricle Parameters

In this study, only the depth parameter related to the lateral ventricles could be evaluated. Accordingly, a significant difference was found in the comparison of the depth parameter between trimester groups ($p<0.05$, Table 5). In the study by Grossmann et al. on fetuses between 25–41 weeks of gestation, it was stated that the volume of the lateral ventricles did not show a significant change with gestational age. In the same study, a comparison by sex was not performed, but the necessity of such an evaluation was emphasized (6). In this study, ventricle depth was assessed in terms of sex, and no significant difference was found. Additionally, no difference was observed between the depths of the right and left ventricles, which, in line with previous studies, indicates that symmetrical growth of the lateral ventricles continues during the fetal period (8). In ventriculomegaly, one of the pathologies encountered during the fetal period, it is reported that while the parenchyma remains within normal limits, the size of the lateral ventricles increases significantly. An increased ratio of ventricle volume to hemisphere volume has been evaluated as a finding in favor of ventriculomegaly (6). Therefore, knowledge of brain and ventricle morphometry during the fetal period may provide significant advantages in prenatal diagnosis.

Since the lateral ventricles are located within the hemispheres, the growth relationship between these two structures has been examined using the ratio of ventricle depth to brain hemisphere depth. According to our findings, these two structures grow proportionally between the 1st–2nd and 3rd trimester-full term; however, between the 2nd and 3rd trimesters, the brain hemispheres were observed to grow more rapidly. The literature indicates that the volume of the lateral ventricles peaks at the 23rd week and subsequently decreases in proportion to brain volume (6,11,30–33). This ratio is higher in the early gestational weeks but decreases relatively in the following weeks due to the increasing growth of cerebral white matter and basal ganglia (7,34).

Conclusion

This study is one of the few studies that evaluates morphometric measurements of the fetal brain hemispheres and lateral ventricles across a wide gestational age range using stereological and linear methods. While in the literature these structures are often evaluated in limited gestational age groups and mostly using in vivo techniques, this study provides a more detailed and continuous developmental profile by using MRI on postmortem fetal specimens.

The study shows that right and left hemisphere development is symmetrical during the fetal period and that the lateral ventricles stabilize in the later weeks of gestation.

The data obtained help fill morphometric gaps between trimesters in the literature and contribute to the determination of normal measurement ranges and prenatal diagnosis, offering a valuable resource particularly for the early detection of fetal CNS anomalies. We believe this study will make significant contributions to the evaluation of central nervous system development, the identification of normal variations, and the early diagnosis and treatment planning of pathological conditions, especially in the fields of obstetrics, perinatology, fetopathology, and pediatrics.

Limitations

Although this study reveals the morphometric development of cerebral structures during the fetal period in detail, it does have certain limitations. Firstly, the use of postmortem fetal materials in the study, along with formaldehyde fixation and potential postmortem tissue changes, does not allow for a full comparison with in vivo data. In addition, the unequal number of samples for each gestational week prevented weekly analyses in some cases. Especially, the limited number of samples from the first trimester (3rd month) and early gestational periods restrict the generalizability of the results for those weeks.

MRI imaging was performed using a 0.2 Tesla device, and due to the low field strength, there were limitations in visualizing certain small anatomical details.

Finally, the study includes only two-dimensional and volumetric measurements; neurodevelopmental parameters such as cortical layering, microstructural development, or functional relationships were not assessed.

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Conflict of interest statement

The authors hold no affiliations or relationships that could give rise to any potential conflicts of interest.

Ethics Committee Approval

The necessary ethical approval for this study was obtained from the Faculty Ethics Committee of Süleyman Demirel University Faculty of Medicine (Decision Date: 13.12.2000, Decision No: 2).

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