THE ASSESSMENT OF THE BIOMETRIC PARAMETERS WITH FETAL MAGNETIC RESONANCE IMAGING IN FETUSES WITH MILD-ISOLATED VENTRICULOMEGALY

Fetal İzole Ventrikülomegalide Biyometrik Parametrelerin Manyetik Rezonans Görüntüleme ile Değerlendirilmesi

Fatma Ceren SARIOĞLU[1], Orkun SARIOĞLU[2], Deniz ÖZTEKİN[3], Özgür ÖZTEKİN[2]

[1]Dokuz Eylül Üniversitesi
Tıp Fakültesi
Radyoloji Anabilim Dalı
Pediatrik Radyoloji Bilim Dalı
İzmir/Türkiye

[2]Sağlık Bilimleri Üniversitesi
Tepecik Eğitim ve Araştırma Hastanesi
Radyoloji Anabilim Dalı
İzmir/Türkiye

[3]İzmir Ege Kadın Hastalıkları ve Doğum Evi
Kadın Hastalıkları ve Doğum Bölümü
İzmir/Türkiye

Fatma Ceren SARIOĞLU, Uzm. Dr. (0000-0002-6714-2367)
Orkun SARIOĞLU, Uzm. Dr. (0000-0003-1173-8046)
Deniz ÖZTEKİN, Doç. Dr. (0000-0002-4213-7254)
Özgür ÖZTEKİN, Prof. Dr. (0000-0002-0092-5260)

İletişim:
Uzm. Dr. Fatma Ceren SARIOĞLU
Dokuz Eylül Üniversitesi Hastanesi, Radyoloji Anabilim Dalı, Pediatrik Radyoloji Bilim Dalı, İzmir/Türkiye
Telefon: +90 505 962 8801
e-mail: drcerenunal@gmail.com

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ÖZET

Amaç: Hafif izole ventrikülomegali tespit edilen fetal olgularda beyin biyometrik parametrelerinin fetal manyetik rezonans görüntüleme (MRG) ile değerlendirilmesidir.

Gereç ve Yöntemler: Antenatal ultrasonda (USG) hafif izole ventrikülomegali tespit edilen ve MRG ile değerlendirilmiş 36 fetüsün MRG görüntüleri retrospektif olarak değerlendirildi. Değerlendirmede fetal beynin tegmento-vermian açısı, vermis anteroposterior ve superoinferior mesafeleri, korpus kallozum uzunluğu, fronto-oksipital mesafe, serebellum transvers mesafesi, serebral ve kalvarial biparietal çap, interhemisferik mesafe, 3. ventrikül genişliği ve sisterna magna mesafesi 2 deneyimli radyolog tarafından birbirlerinden bağımsız olarak ölçüldü. Ölçümler çeşitli sebeplerle MRG çekilmiş ancak herhangi bir santral sistemi anomalisi bulunmayan, 34 normal fetüsün beyin biyometrik ölçümleri ile karşılaştırıldı. P değerinin <0.05 olması anlamlı kabul edildi.

Bulgular: Hafif-izole ventrikülomegali olguları ile kontrol grubunun gestasyonel yaşları arasında anlamlı farklılık saptanmadı (gestasyonel yaşlar sırasıyla 24.73 ± 0.60,24.52 ± 0.64, p=0.595). İki grubun beyin biyometrik ölçümleri kıyaslandığında anlamlı farklılık saptanmadı (p> 0.05). Her iki grupta da vermis anteroposterior ve superoinferior mesafeleri, korpus kallozum uzunluğu, fronto-oksipital mesafe, serebellum transvers mesafesi, serebral ve kalvarial biparietal çap, interhemisferik mesafe, 3. ventrikül genişliği ve sisterna magna mesafesinin gestasyonel yaş ile birlikte artış gösterdiği, tegmento-vermian açının ise azaldığı saptandı. İnterhemisferik mesafe ve 3. ventrikül genişliği gebelik boyunca her iki grupta da stabil iken, hafif-izole ventrikülomegali grubunda sisterna magna mesafesinin gestasyonel yaş arttıkça artma eğiliminde olduğu görüldü.

Sonuç: Çalışmamızda normal ve izole VM grupları arasında beyin biyometrik değerlerinde farklılık bulunmamıştır. VM'li fetüslerde fetal MRG eşlik eden patolojileri ve normal intrakraniyal anatomiyi değerlendirmek için kullanılmaktadır. Daha doğru sonuçlara ulaşmak için ileri çalışmalar gereklidir.

Anahtar Kelimeler: *Biometri; Fetal; Manyetik rezonans görüntüleme; Prenatal; Ventrikülomegali*

ABSTRACT

Objective: To evaluate the biometric parameters of fetal brain in mild-isolated ventriculomegaly (VM) by using fetal brain magnetic resonance imaging (MRI).

Material and Methods: In this retrospective study, we reviewed the fetal brain biometry in 36 fetuses with mild-isolated VM and 34 fetuses who had no central nervous system abnormality by using MRI. All the images were interpreted by two radiologists. The evaluated parameters of both groups were tegmento-vermian angle, anteroposterior and superoinferior diameter of vermis, length of the corpus callosum, fronto-occipital diameter, laterolateral diameter of the cerebellum, cerebral and calvarial biparietal diameter, width of interhemispheric distance, third ventricle, and cisterna magna.

Results: The mean gestational age was not significantly different between the normal group and mild-isolated VM group 24.73 (SD ± 0.60) and 24.52 (SD ± 0.64), respectively (p=0.595). No statistically significant difference was found in biometric parameters between the groups (p > 0.05). The anteroposterior and superoinferior diameter of the vermis, length of the corpus callosum, fronto-occipital diameter, cerebellar laterolateral diameter, cerebral and calvarial biparietal diameter increased and tegmento-vermian angle decreased with gestational age. Interhemispheric distance and third ventricle diameter were stable in both groups, and the width of cisterna magna also was stable in the normal group, while tended to be increased in the mild-isolated VM group.

Conclusion: Intracranial anatomy should be evaluated carefully in fetuses with VM to rule out associated abnormalities although no differences in biometric values between normal and isolated VM groups in our study. Further studies are required to reach more accurate results.

Keywords: *Biometry; Fetal; Magnetic Resonance Imaging; Prenatal; Ventriculomegaly.*

INTRODUCTION

Ventriculomegaly (VM) is one of the most frequent type of central nervous system (CNS) abnormalities. VM is defined as a transverse atrial diameter of lateral ventricle is higher than 10 mm at any gestational age. Fetal VM has been divided in three groups: mild VM (10-12mm), moderate (12.1-15 mm), and severe VM (>15 mm) (1). VM can be associated with anomalies of CNS such as obstructive pathologies, dysgenesis of some structures such as dysgenesis of corpus callosum or holoprosencephaly and destructive pathologies. VM is also seen as an isolated form which is not associated with any CNS anomalies. VM which is associated with other CNS anomalies, has a high risk of a poor neurologic outcome of the fetuses (2).

Evaluation of the fetal CNS is limited by ultrasound due to the fetal position, maternal causes, technical causes as well as the experience of sonographer. Also, measurements of fetal structures may vary depending on the fetal position, skull ossification, and preference of sonographer. On magnetic resonance imaging (MRI), images are planned with considering the fetal position. MRI allows for complete visualization of the ventricles and brain parenchyma without positional artifacts. MRI is increasingly being used to evaluate the fetal brain and is a valuable complement to prenatal ultrasound. Many studies showed that fetal MRI is more sensitive and specific to detect many of the fetal CNS abnormalities associated with VM (3–6). It also provides more accurate quantifications and analysis in measuring of biometric values. The importance of the knowledge of biometric values is an essential criteria in follow-up during pregnancy.

In this retrospective study, we aimed to evaluate the biometric parameters of fetal brain in mild-isolated VM and compare them with normal group by using fetal brain MRI.

MATERIALS and METHODS

Subjects

The study was approved by the local ethics committee. The patients who had VM in ultrasonography and underwent fetal MRI between January 2014 and January 2016 were scanned retrospectively from our local archive in this study. Inclusion criteria were mild-isolated VM detected on MRI and gestational age from 20 to 34 weeks. The gestational ages of the study groups were considered based on the last menstrual period. All the fetuses were referred after an ultrasound examination and the gestational age was confirmed by a first trimester ultrasound examination. Fetuses with poor imaging qualities due to the motion artifacts (n = 5), CNS anomalies (n = 3), abnormal genetic tests (n = 2), and images that were not contain optimal axial, coronal, and sagittal slices (n = 7) were excluded. Multiple pregnancies (n =1) were excluded as well. All blood samples were analyzed for TORCH titers. One patient who had high titer concerning of CMV was also excluded. After the exclusion criteria, 36 fetuses with mild-isolated VM were included in our study. Control group consisted of children who performed with fetal MRI due to several causes and with normal CNS MRI findings. There were 34 normal fetuses who composed of normal group.

MRI protocols

MRI examinations with standard protocol were performed by 1.5 T MRI systems (Siemens Avanto, Siemens Aera, GE Optima360) using a 6-channel body coil with a radiologist monitoring. Images were acquired with T2-weighted MRI sequences: fast imaging with steady-state free precession (true FISP) and half-Fourier acquisition single-shot turbo spin-echo (HASTE). Fetal brain images were performed using both techniques in axial, coronal, and sagittal planes to the fetal brain. The parameters for HASTE imaging included time to repetition (TR): 1350 ms; time to echo (TE): 84ms; flip angle (FA): 120 degrees; slice thickness: 5 mm; matrix: 256 × 256; NSA:1. The parameters of true FISP imaging were TR: 4.4ms, TE: 2.2ms, slice thickness: 5mm, matrix: 240 × 256; NSA:1. MRI was performed without sedation or contrast agent.

Image interpretation

All of the control group and mild-isolated VM group was evaluated for biometric parameters of fetal brain. VM was defined as mild when the atrial width is 10-12mm. If the presence of asymmetric VM, the definition was considered according to the larger ventricle. The evaluated parameters of both groups were tegmento-vermian angle, anteroposterior and superoinferior diameter of vermis, length of the corpus callosum, fronto-occipital diameter (FOD), laterolateral diameter of the cerebellum, cerebral and calvarial biparietal dia-

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meter (BPD), width of interhemispheric distance, third ventricle, and cisterna magna. The biometric values were measured according to a book published by Garel (7) and a study of Parazzini et al. (8) (Figure 1). The ventricular atrial diameter was measured on axial sections at the level of the posterior margin of the choroid plexus. When ventricular size was measured asymmetrically, the size of larger ventricle was used for analysis. The axial sections were also used for measurement of the width of cisterna magna (between the basis of the vermis and inner table of occipital bone). The coronal sections through the temporal horn of lateral ventricles were used for measurement of cerebral BPD (between the two outer margins of frontal cortex) and calvarial BPD (between both inner tables of frontal bones), the width of interhemispheric distance, and third ventricle. Laterolateral diameter of the cerebellum was also measured at the coronal section at the level of occipital horn of the lateral ventricle. The sagittal sections were used for measurement of TVA (between the anterior wall of the fourth ventricle and inner margin of the vermis), anteroposterior and superoinferior diameter of vermis (the greatest distance from the fastigium to the posterior surface of the vermis and the highest height), length of the corpus callosum (between the anterior and posterior inner surface) and FOD.

The best sections were chosen for evaluation. All of the images were interpreted, and all the parameters were measured by 2 years-experienced pediatric radiologist (F.C.S) and 20 years-experienced neuroradiologist (O.O). All patient data were hidden during the image analysis. The readers evaluated the images and recorded the measurement of all of the fetuses' biometric values.

Statistical analysis

Statistical analysis was performed using IBM SPSS ver. 22.0 (IBM Corp., Armonk, NY, USA). The normality of the variables was analyzed using the Shapiro–Wilk test. Independent samples t-test was used for the analysis of parametric variables while Mann-Whitney U-tests was used for the analysis of nonparametric variables based on the distribution pattern of the data. P value was considered significant when <0.05. Inter-rater

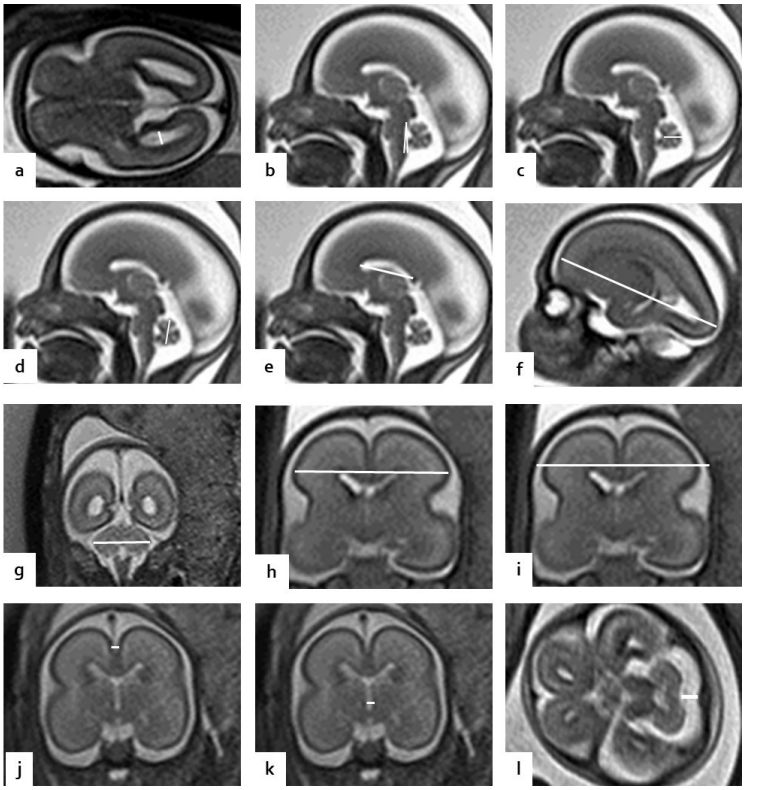
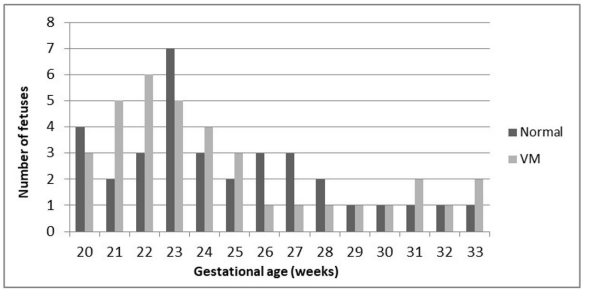


Figure 1. a) The atrial width of lateral ventricle, b) Tegmento-vermian angle, c) Anteroposterior diameter of vermis, d) Superoinferior diameter of vermis, e) Length of the corpus callosum, f) Fronto-occipital diameter, g) Laterolateral diameter of the cerebellum, h) Cerebral biparietal diameter, i) Calvarial biparietal diameter, j) Width of interhemispheric distance, k) Width of third ventricle, and l) Width of cisterna magna

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Figure 2. Gestational age distributions of normal and ventriculomegaly groups



agreement assessed using the intra-class correlation coefficient (ICC). The degree of interobserver agreement was excellent in the measurement of biometric values (ICC= 0.913-0.944, 95 % Confidence interval 0.838-0.981). Thus, measurements were recorded according to the averages of observers' results.

RESULTS

This retrospective study presents the comparison of biometric values of fetal brain parameters between normal group (n = 34) and mild-isolated VM group (n = 36). There were no statistical differences of the mean gestational age of normal group and mild-isolated VM group 24.73 (SD ± 0.60) and 24.52 (SD ± 0.64), respectively (p = 0.595). The mean age of mothers of normal group and mild-isolated VM group 28.55 (SD ± 1.00) and 29.63 (SD ± 0.95), respectively (p = 0.437). The ventricular size was significantly different between normal group and mild-isolated VM group (p < 0.001). The larger ventricular size was 6.15 (SD ± 0.18) in normal group while 11.38 (SD ± 0.14) mild-isolated VM group. The distribution of the number of normal and mild-isolated VM fetuses as a function of gestational age was demonstrated as a histogram in Figure 2. The measurements of the biometric values of both groups are shown in Table 1. Our analysis showed no statistically significant difference in biometric values of these groups. Anteroposterior and superoinferior diameter of vermis, length of the corpus callosum, FOD, cerebellar laterolateral diameter, cerebral and calvarial BPD increased and tegmento-vermian angle decreased with gestational age as they are seen in the graphics (Figure 3). Interhemispheric distance and third ventricle diameter tended to be constant while the gestational age increased. Width of cisterna magna also was stable in normal group, while tended to be increased in the study group (Figure 4).

DISCUSSION

This retrospective study presents the comparison of fetal brain parameters between normal group (n=34) and mild-isolated VM group (n=36) on MRI. Statistical analysis did not reveal any significant difference of biometric parameters between normal and mild-isolated VM groups.

Fetal VM has a remarkably diverse etiology; it can be isolated or associated with other CNS anomalies. When the fetal VM is determined, causes of VM related to CNS anomalies should be excluded. Many studies show that MRI provides more information about fetal CNS following normal ultrasound findings. Additionally, more accurate quantifications and analysis in measuring of biometric values can be obtained by using MRI.

Fetal biometric parameters for reference charts had been established in different ethnic groups in the literature. Additionally, there have been several articles about biometric parameters of fetal brain by 2D or 3D measurements with using MRI (8–13). Comprehensive researches on fetal biometry indicate the importance of biometric measurements in the follow-up of normal fetal brain development. Tilea et al. (10) presented a systematic review and created a reference chart and formula for cerebral MRI biometry at 26–40 weeks'. Previous reports (8,10,12,13) have found that the cerebral BPD, FOD, cerebellar laterolateral diameter, the height of vermis and anteroposterior diameter of the vermis, length of the corpus callosum increased with gestational age. Parazzini et al. (8) also reported that the width of interhemispheric distance and third ventricle are relatively stable while increasing of gestational age. These findings are compatible with our results.

Interestingly, cisterna magna tended to be increased with gestational age in mild-isolated VM group in contrast to normal group although no significant difference was found between these groups in our study. We speculate that the increased diameter of cisterna magna may be explained with increased CSF in the VM group. Besides, Brown (14) suggested that the width of cisterna magna has been increased with gestational age. It is possible to reach more accurate

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results with area measurement as in a study of Ber et al. (15) which demonstrated the increasing of the area of cisterna magna with gestational age. There are few studies in the literature investigating whether fetuses with isolated VM have differences in biometric measurements (11,16). In a study of Fishel-Bartal et al. (16), the authors measured the biometric parameters with ultrasonography. When we compared our data with those by Fishel-Bartal et al. (16), we observed differences of fetal biometry by MRI, while no substantial differences the measurements of FOD, the width of cisterna magna, length of corpus callosum between the study and control group as in their study. In contrast to our research,

Table 1. The measurements of the biometric values of normal and ventriculomegaly group.

	Group	Minimum	Maximum	Mean ± Std. Deviation	*P* value
TVA	Normal	2,7	11,5	5,274 ± **0,3415**	0.332
	VM	2,2	8,8	5,397 ± **0,2753**	
Vermis AP	Normal	4,2	12,1	7,741 ± **0,3**632	0.569
	VM	3,9	15,4	7,689 ± **0,4542**	
Vermis SI	Normal	7,9	18,3	12,462 ± 0,5104	0.638
	VM	5,9	20,1	12,086 ± 0,6024	
Length of CC	Normal	12,2	35,0	24,909 ± **1**,0377	0.900
	VM	10,3	35,1	24,728 ± 0,9963	
FOD	Normal	47,3	89	68,812 ± 2,0286	0.932
	VM	45,4	105,9	69,083 ± 2,4380	
LL cerebellum	Normal	16,5	33,7	26,415 ± **0**,8259	0.338
	VM	16,3	44,4	25,847 ± 1,1107	
BPD (cerebrum)	Normal	33,0	65,2	49,865 ± 1,5770	0.950
	VM	34,5	73,7	50,003 ± 1,5399	
BPD (calvarium)	Normal	40,6	70,2	58,000 ± 1,6496	0.755
	VM	40,5	80,1	57,514 ± **1,5856**	
IHD	Normal	1,1	3,1	2,115 ± **0**,0836	0.699
	VM	0,9	3,2	2,164 ± **0**,0943	
Third ventricle	Normal	1,2	3,5	2,197 ± **0**,9500	0.472
	VM	1,5	4,0	2,347 ± **0**,0992	
Width of CM	Normal	4,3	9,0	6,215 ± **0**,1804	0.223
	VM	4,0	9,0	6,592 ± **0,2442**	

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they found a significantly larger BPD in isolated VM group. This may be related to the calculation of BPD in cranial ultrasound according to the measurements of the skull but based on brain tissue measurements in fetal MRI. Grossman et al. (11) studied the volumetric parameters of fetal brain in normal and VM groups and found that there were no significant differences in parenchyma volume between these groups. Their probable explanation for this situation was to allow the growing of brain parenchyma by unclosed sutures in fetuses with VM. Despite the fact that our study is not directly comparable with that of Grossman et al. (11) because of using different methods, it may be assessed as an interrelated result. We also added the measurement of tegmento-vermian angle because it is an important measurable parameter in the assessment of posterior fossa abnormalities in the fetus (17). Previous studies which provide the reference charts of biometric parameters did not investigate the normal reference value of tegmento-vermian angle. The tegmento-vermian angle is considered to be as normal when close to 0 degrees (17). Fetuses with high tegmento-vermian angle should be evaluated for posterior fossa anomaly. Volpe et al. (18) reported the ultrasonographic measurement of the tegmento-vermian angle between 4-17 (mean 9.1) degree in their study which included 80 normal fetuses at 20–24 weeks' gestation. Comparing our results, mean tegmento-vermian angle was lower in both control and normal groups in our study. Additionally, we found a decreased tegmento-vermian angle degree with increasing of gestational age.

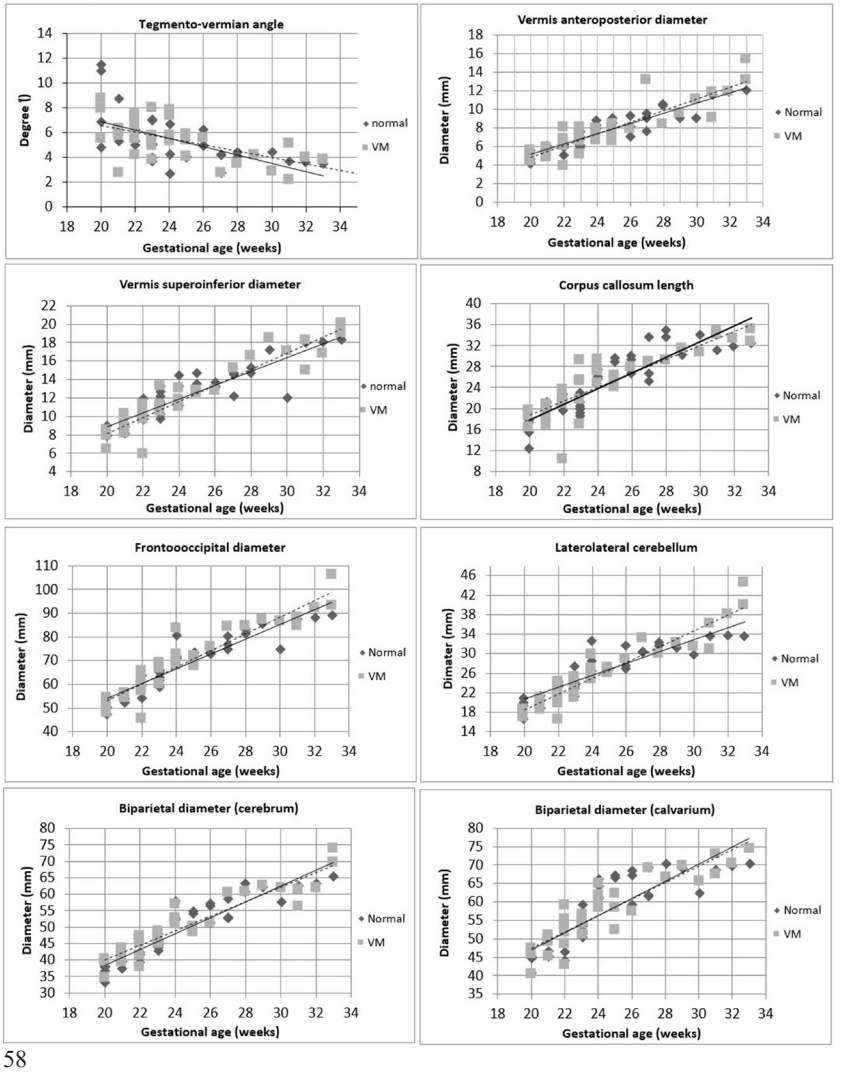


Figure 3. Scatter plots show tegmento-vermian angle, vermis anteroposterior and superoinferior diameter, length of the corpus callosum, fronto-occipital diameter (FOD), cerebellar laterolateral diameter, and cerebral and calvarial biparietal diameter in relation to gestational age in normal and isolated-mild ventriculomegaly groups. Tegmento-vermian angle decreases; however, anteroposterior and superoinferior diameter of vermis, length of the corpus callosum, FOD, cerebellar laterolateral diameter, cerebral and calvarial BPD increases with gestational age in both groups.

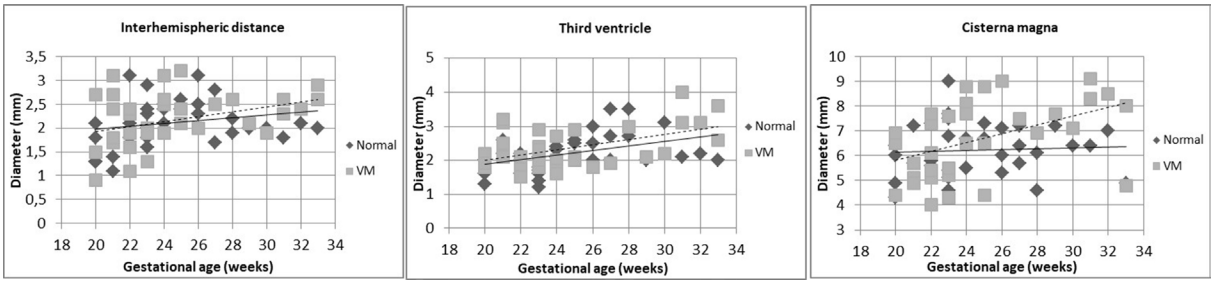


Figure 4. Scatter plot show interhemispheric distance, third ventricle diameter, and width of cisterna magna in relation to gestational age in normal and isolated-mild ventriculomegaly groups. Interhemispheric distance and third ventricle diameter are constant while the gestational age increase. The width of cisterna magna is stable in the normal group, while increase in the ventriculomegaly group.

As stated in many previous studies, fetuses with isolated VM, in particular, mild-isolated VM, have good prognosis in contrary to VM associated with CNS anomalies. The range of prognosis of mild-isolated VM has been varied in different studies. In a systematic review by Pagani et al. (19) showed that the prevalence of neurodevelopmental delay was 7.9% in fetuses with mild-isolated VM. Furthermore, in the prospective study by Bar-Yosef et al. (20) reported that a normal neurodevelopmental outcome is to be expected in fetuses with isolated VM. In addition, the absence of CNS anomalies, a good or normal fetal outcome in isolated VM may be associated with the normal development of cerebral and cerebellar structures which are shown by using the biometric parameters.

The main problems and limitations in our study are following, the fetuses were not followed due to the retrospective study. Besides, some of the patients who had eligible sagittal and axial sections but not have perfect midsagittal section were excluded because the length of the corpus callosum and tegmento-vermian angle were not measured accurately. Third ventricle and interhemispheric distance are considerably small-sized, so their measurements were performed difficultly. However, the correlation was excellent between the observers' results. The other limitation was the slice thickness of 5 mm. Despite some problems of measurements, MR imaging ensures more certain measurements compared to ultrasonography. Although the volume measurements provide more accurate results, we did not perform a volumetric analysis since we thought that the slice thickness of our MR imaging protocol was not eligible for reliable volumetric analyses. Because this study aimed to evaluate the fetal brain biometric measurements on MR imaging in fetuses with mild-isolated VM, no analysis of the neonatal outcome was performed.

CONCLUSION

Our study indicates no differences in biometric values between normal fetuses and fetuses with mild-isolated VM. A larger patient population and long-term follow-up are exactly required for more accurate results. It should not be forgotten that while fetuses with mild-isolated VM appear to have 2D MR imaging intracranial biometric measurements similar to normal fetuses, an accurate evaluation of the fetal intracranial anatomy is still necessary to rule out possible abnormalities that may be associated with or represent the cause of cerebral VM.

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