

Posterior fossa assessment in the axial view of the head at 11-14 weeks of gestation in normal and aneuploid fetuses

MONA ELENA ZVANCA¹, ALEXANDRA MUNTEANU¹, MIHAELA BOT¹,
AIDA PETCA¹ and DRAGOS NEMESCU²

¹Department of Obstetrics and Gynecology, 'Carol Davila' University of Medicine and Pharmacy, Elias University Hospital, 011461 Bucharest; ²Department of Obstetrics and Gynecology, 'Grigore T. Popa' University of Medicine and Pharmacy, 700115 Iasi, Romania

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Abstract. Posterior fossa ultrasound appearance may offer clues for brain anomalies as early as the first trimester. The purpose of the study was to find an easy, reproducible method to examine the posterior fossa. From January 2017 to March 2018, 132 consecutive pregnancies presenting for first-trimester screening, were selected at 11-14 weeks' gestation. An oblique axial view of the fetal head was routinely achieved with visualization of the posterior fossa, wherein the cisterna magna (CM) and the fourth ventricle (V4) antero-posterior diameter was measured. Moreover, 81 patients had a follow-up scan at 19-24 weeks, and the CM and transverse cerebellar diameter (TCD) were measured. Normal ranges were established at 11-14 weeks for CM and V4 according to crown-rump length (CRL). The 50th centile for CM ranges from 1.2 mm to 2.3 mm at a CRL between 45 and 85 mm. The V4 50th centile ranges from 1.8 to 2.4 mm. A positive correlation was found between the first-trimester and second-trimester CM diameter and between the first-trimester V4 and second-trimester TCD. There is an inverse correlation between the first-trimester CM and second-trimester TCD. The measurements of different components of the posterior fossa in the first trimester cannot predict the size of CM and TCD in the second trimester. The presence of the three hypoechoic structures (cerebral peduncles, V4, and CM) separated by two hyperechoic lines is easy to see and measure.

Introduction

The first-trimester visualization and analysis of the fetal brain has become a reality in recent years, thanks to technological

advancements that allow superimposing theoretical knowledge of early fetal development with sonographic images of different fetal stages. The road was opened in 2009 by Chaoui *et al* (1) in search of early signs of open spina bifida, and for several years, this was the only direction for clinical research (2-4). The detailed description of the posterior fossa allowed the identification and pursuing the development of different anatomical structures, from 11 weeks to later in the second trimester. The initial description of 'intracranial translucency' was later abandoned as it became clear that the structure was the V4. Standard measurements were performed using the already standard sagittal section of the fetal head, with the described landmarks for the nuchal translucency assessment. However, using just the fetal head mid-sagittal plane, specific intracranial structures, especially supratentorial, cannot be seen, and their development cannot be assessed. We need axial, as well as oblique head sections, for a thorough examination of the fetal brain. Therefore, the standardization of these sections and measurements is mandatory.

Patients and methods

From January 2017 to March 2018, all women with a viable pregnancy presenting for first-trimester screening were included in the study. Both singleton and multiple pregnancies were included, provided that a proper examination of all the fetuses was possible. The main inclusion criteria were fetal crown-rump length (CRL) between 45-84 mm and patient consent for additional measurements during the standard fetal examination. Cases were excluded when fetal anatomical assessment was suboptimal. The analysis included fetuses with structural defects which were examined separately. The study was conducted in accordance with the World Medical Association's Declaration of Helsinki. The pregnant women included in the study provided written informed consent and the study protocol was approved by the Ethics Committee of the Elias University Hospital (Bucharest, Romania).

After nuchal translucency (NT) measurement, the probe was rotated by 90°, and a transverse section of the fetal head was obtained. The probe needs to be slightly tilted to the point where the posterior fossa becomes visible. At this level, three hypoechoic spaces are visible, separated by echogenic

Correspondence to: Dr Dragos Nemescu, Department of Obstetrics and Gynecology, 'Grigore T. Popa' University of Medicine and Pharmacy, 16 Universitatii Street, 700115 Iasi, Romania
E-mail: dragos.nemescu@umfiiasi.ro

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Table I. Summary of the main maternal characteristics, ultrasound measurements, biochemistry results and estimated risks for the main aneuploidies.

Variables	Minimum	Mean	Maximum
Maternal age (years)	20	30.66	45
Maternal weight (kg)	41.5	59.65	84.0
CRL (mm)	47.6	63.65	81.3
NT (mm)	1.1	1.89	5.9
DV PI	0.8	1.1	2.1
β -hCG MoM	0.236	1.236	5.220
PAPP-A MoM	0.202	1.025	2.513
Risk for T21	1/30,664	1/15-966	1/2
Risk for T18	1/361,907	1/191-525	1/136
Risk for T13	1/851,951	1/426-932	1/10

CRL, crown-rump length; NT, nuchal translucency; DV PI, ductus venosus pulsatility index; hCG, human chorionic gonadotropin; MoM, multiple of median; PAPP-A, pregnancy associated placental protein A; T21, trisomy 21; T18, trisomy 18; T13, trisomy 13.



Figure 1. Axial view of the fetal posterior fossa with measurements of the CM (down) and V4 (up). CM, cisterna magna; V4, fourth ventricle.

lines. From anterior to posterior, these spaces are the thalamic nuclei and the cerebral peduncles, fourth ventricle (V4) and cisterna magna. These structures find their correspondent on the mid-sagittal section of the fetal head.

The anteroposterior diameter of the V4 and the cisterna magna (CM) were measured on an axial view of the posterior fossa (Fig. 1). All measurements were performed during the fetal examination, and no post-processing was required.

A second fetal assessment, was performed routinely between 19-24 weeks of gestation, measuring the CM width and transverse cerebellar diameter (TCD) as previously described (5-7).

All ultrasound examinations were performed on Voluson E8 Expert or V730 ultrasound machines (GE Healthcare), by a single operator (MZ). A transabdominal or transvaginal approach was used, as required for a better evaluation of the fetal anatomy.

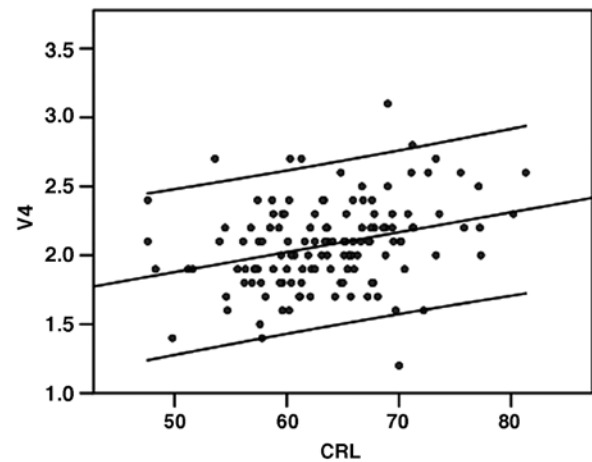


Figure 2. Distribution of the transverse diameter of V4 according to CRL. V4, fourth ventricle; CRL, crown-rump length.

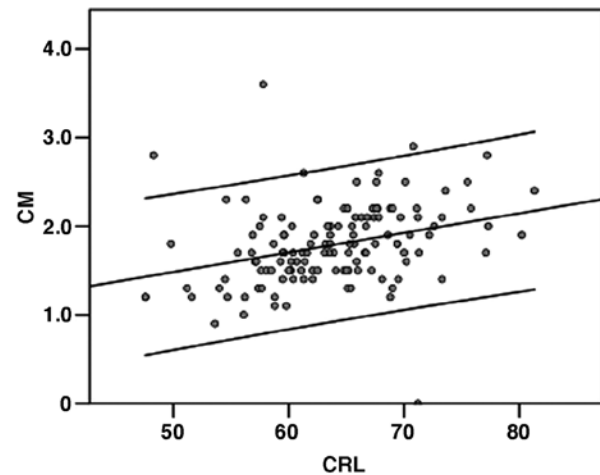


Figure 3. Distribution of the measurements of the CM according to CRL. CM, cisterna magna; CRL, crown-rump length.

Statistical software package SPSS 23.0 (SPSS Inc.) was used for data analyses. The normality of distribution was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Continuous variables were compared using the t-test for independent means. Correlation between study variables was verified using Pearson's correlation coefficient. P-value <0.05 was considered statistically significant.

Results

At the time of the first-trimester scan 132 fetuses were evaluated. The primary maternal characteristics, ultrasound measurements, biochemistry results, and the estimated risks of aneuploidies are detailed in Table I. Both maternal and fetal population were normally distributed according to the CRL measurements and maternal age.

The size of the V4 had a mean of 2.076 mm (range 1.2-3.1 mm) and was significantly correlated with CRL ($P < 0.01$), according to Pearson r assumption for a normally distributed population. Its 50th centile varies from 1.8 mm at a CRL of 45-2.4 mm at a CRL of 84 mm (Fig. 2).

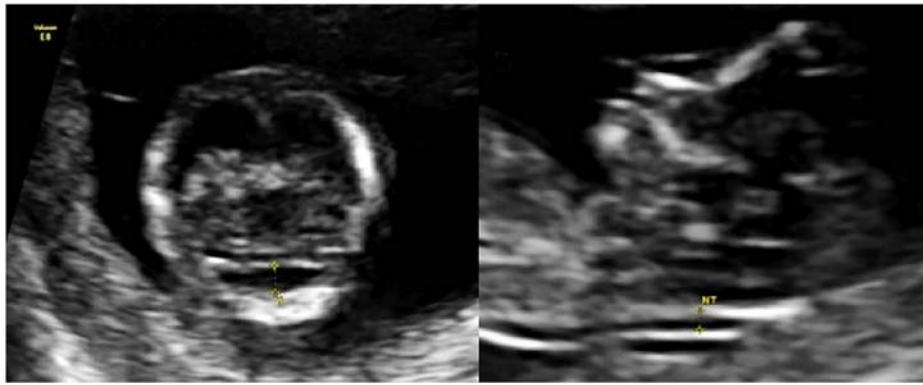


Figure 4. Axial (left) and mid-sagittal (right) view of the fetal head, in a fetus with trisomy 13. The normal anatomy of the posterior fossa is distorted, with increased size of V4 and unmeasurable CM. The measurements are better performed on transversal plane. V4, fourth ventricle; CM, cisterna magna.

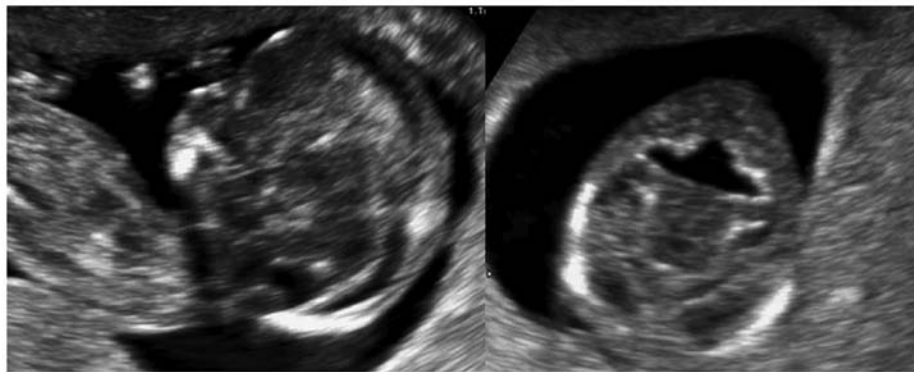


Figure 5. The posterior fossa in mid-sagittal (left) and axial (right) view, in a fetus with diandric triploidy. The amount of fluid is generally increased, but there is no separation of the V4 and CM. V4, fourth ventricle; CM, cisterna magna.

The CM measurements had a mean of 1.784 (range 0-3.6 mm) and CM was significantly correlated with CRL ($P < 0.01$). The 50th centile for CM varies from 1.2 mm at a CRL of 45-2.3 mm and at a CRL of 84 mm (Fig. 3).

For 81 fetuses, the follow up at 19-24 gestational weeks was possible. In this group, the Pearson r coefficient indicated a positive correlation between the first-trimester and second-trimester measurement of CM, which is not statistically significant ($P = 0.465$).

Comparing the development of the CM and the V4 between 11 to 14 gestational weeks, it was noted that the size of the CM is inferior to V4, at the same gestational age. However, its growth is faster, and it will intersect and surpass the development of the V4 after the first trimester. There was no correlation between the size of V4 or CM and maternal characteristics.

It was found that there is a low positive correlation between the first-trimester V4 measurements and the second-trimester TCD, and an inverse correlation between the first-trimester CM and the second-trimester TCD, the results are not statistically significant.

In the study group, there were a series of cases with genetic and structural anomalies, in which possible early deviations in the morphology of the posterior fetal fossa were analyzed.

There were two cases with confirmed trisomy 21. In both, the anteroposterior diameter of the V4 was equal to the CM diameter (2.2 mm and 2.3 mm, respectively). All measurements were within the normal range for CRL.

In one case of trisomy 13, the measurement of V4 was 2.8 mm, and the CM was unmeasurable (0 mm). There was no spinal defect in this case. At a CRL of 70 mm, the size of the V4 is above the 95th centile. When comparing the images of the posterior fossa in the mid-sagittal and axial views, the measurements of the two components are more comfortable to perform, and more evident in the transversal plane (Fig. 4).

In a fetus with trisomy 18, with a CRL of 50.5 mm, the measurement of the V4 was 2.5 mm, which is the 95th centile. The CM size was 1 mm, which is just above the 5th centile for gestational age. The measurements were performed by the transabdominal approach, but the discrepancy in the size of the two structures is better seen using the transvaginal probe.

In one case of diandric triploidy, the distortion of the posterior fossa was so marked that no reliable measurement was possible. The separation between the V4 and CM was not identifiable, probably due to a significant delay in vermillion development (Fig. 5). No case of open spina bifida was found in our series.

Discussion

In literature only one large prospective study was found, including 692 first-trimester fetuses in which the posterior fossa was assessed in the axial view of the head (8). The operators measured the anteroposterior diameter of the V4, CM and TCD on acquired ultrasound volumes of the fetal head. In their

study, the 50th centile for CM ranges from 1 mm at a CRL of 45-3 mm and at a CRL of 85 mm. The 50th centile of the V4 ranges from 1.7 to 2.4 mm. Even though the variation range in the study of Egle *et al* (8) is narrower than in our study, we have seen a similar trend in the development of the two structures, with V4 larger at lower CRL and a steeper increment in the diameter of cisterna magna as the first trimester comes to an end. The differences between the present results and these measurements may be explained by a different technique, as well as by a larger number of cases.

Papastefanou *et al* (9) established references for CM and V4 measurements in the mid-sagittal view of the fetal head, at the end of the first trimester, on 465 fetuses with known outcome.

If we compare the V4 and CM measurements in the mid-sagittal and axial views, as plotted in the two previous studies, they are superimposable. The 50th centile for CM on the sagittal plane ranges from 0.9 to 2.8 mm, and on transverse plane varies from 1 to 2.8 mm. The 50th centile for the diameter of the V4 on sagittal view ranges from 1.5 to 2 mm and on the transversal view ranges from 1.7 to 2.2 mm.

Loureiro *et al* (10) used volumetric acquisitions in order to measure the diameter of the V4 on axial views, in a study that was focused on the assessment of morphologic differences of the posterior fossa between euploid and aneuploid fetuses. They compared 62 fetuses with trisomy 21, trisomy 13, trisomy 18, and triploidy, to 410 euploid fetuses. The fetuses with trisomy 13, 18, and triploidy, had an increased transverse diameter of the V4, whereas, in fetuses with trisomy 21, the measurements resembled euploid fetuses.

A similar conclusion was drawn from other studies that assessed the posterior fossa at 11-14 gestational weeks, but the measurements were performed in the mid-sagittal plane. Ferreira *et al* (11) measured the brain stem diameter (BS) and the distance between the brain stem and occipital bone (BSOB). In trisomy 13, trisomy 18, and triploidy, the BS diameter and BS to BSOB ratio were significantly lower than in euploid fetuses. Assessment of the posterior fossa in a mid-sagittal plane at the time of the nuchal translucency measurement and on the same section of the fetal head was realized by Volpe *et al* (12). They suggest that the increased amount of fluid, mainly when associated with loss of the normal anatomy and normal septation in this area, may be a significant risk factor for future cystic anomalies of the posterior fossa and should prompt further detailed investigations.

The increased amount of fluid in the posterior fossa, starting as early as 11-14 weeks of gestation, is presumed to be related to altered cerebellar and especially vermian development, which is more frequently associated with aneuploidies such as trisomy 18 and 13.

In conclusion, assessment of the anatomical details and measurements of different structures may be performed with similar accuracy on both mid-sagittal and axial views of the fetal head. The results of our study and the anomalies observed and described in specific clinical cases are in line with the published data regarding the anatomy of the posterior fetal fossa at 11-14 weeks. From our experience, assessment of the posterior fetal fossa on the transverse section is feasible even in situations where a perfect sagittal section cannot be obtained.

Assessment of the fetal brain in the axial plane represents an additional step in the first-trimester examination, but it is utterly necessary for a detailed assessment, especially in cases with suspected structural or genetic anomalies. We consider that a skilled practitioner should be able to recognize the details of normal fetal anatomy in both transverse and sagittal planes.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

MEZ designed the study protocol and performed all measurements within the study. AM, MB and AP were involved in the recruitment of the patients and provided care to all the patients included in the study. MEZ and DN performed data analysis. MEZ, AM, MB, AP and DN wrote the manuscript. MEZ and DN participated in the review process, prepared the manuscript, and made substantial intellectual contributions. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present study was conducted in accordance with the World Medical Association's Declaration of Helsinki. The pregnant women included in the study provided written informed consent and the study protocol was approved by the Ethics Committee of the Elias University Hospital (Bucharest, Romania).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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