

First Trimester Neurosonogram-Our Experience

MARIA-CRISTINA COMĂNESCU¹, RĂZVAN GRIGORAȘ CĂPITĂNESCU²,
ALEXANDRU CRISTIAN COMĂNESCU², NICOLAE CERNEA², AURA POPA¹,
ELENA MĂDĂLINA BARBU¹, DANA MARIA ALBULESCU³

¹PhD Researcher, University of Medicine and Pharmacy of Craiova, Romania

²Department of Obstetrics and Gynecology, University of Medicine and Pharmacy of Craiova, Romania

³Department of Anatomy, University of Medicine and Pharmacy of Craiova, Romania

ABSTRACT: Central nervous system (CNS) malformations represent 1% of all births. For this reason, efforts are being made to increase detection of such anomalies prenatally. Consequently, a detailed assessment of the fetal nervous system in the first trimester of pregnancy is no longer a utopia as this kind of evaluation can detect severe malformation such as acrania, neural tube defects, holoprosencephaly or can draw attention regarding to anomalies currently detected in the second trimester due to certain markers of diagnosis. Material and methods: The study included 1376 pregnant women with gestational ages between 11 and 14 weeks, who were referred to our unit for sonographic evaluation. We analyzed in all patients the fetal brain in axial and mid-sagittal views, assessing markers like intracranial translucency, brainstem/brainstem-occipital bone (BS/BSOB) ratio, choroid plexus (CP/HA) ratio, the octopus sign in order to detect as many anomalies in the first trimester of pregnancy. Results: We detected 6 CNS anomalies during our search. All markers assessed were abnormal in all pathological cases. Conclusion: A detailed assessment of the fetal brain is recommended at 11-14 weeks because the earlier the diagnosis is confirmed, the lower the chances of obstetrical, psychological complications to supervene.

KEYWORDS: First trimester scan, neurosonography, CNS malformations

Introduction

Due to the widespread use of the antenatal ultrasound nowadays, we are diagnosing an increasing number of fetal central nervous system (CNS) anomalies prenatally.

If at first the equipment provided only the detection of gross anomalies, recent evolution of ultrasound devices enables more subtle diagnosis of most of the fetal brain disorders.

In spite of the fact that some malformations are detected only in the late third trimester, there is a trend towards a detailed neurosonogram even since the first trimester of pregnancy [1].

CNS anomalies happen in 1% of all births and almost 10% of all malformations detected during perinatal autopsy series are due to CNS disorders.

The detection of a fetal CNS anomaly requires a multidisciplinary approach and, in some cases, patients may benefit from evaluation, delivery and neonatal work-up in a tertiary care center.

Neurodevelopmental follow-up of neonates with CNS disorders is compulsory and should be done by qualified developmental neurologists [1].

The role of the first trimester ultrasound examination has increased in scope from its screening for aneuploidies character to a very important diagnostic tool.

Although all the guidelines recommend fetal neurosonographic assessment in the second trimester, endeavors are made to decrease the gestational age of such sonographic evaluation as low as possible [2].

The assessment of the fetal central nervous system in the first trimester (11-14 weeks) is significant, as several vital anomalies such as anencephaly and holoprosencephaly can be easily detected at this evaluation.

Still, subtle anomalies like neural tube defects, encephaloceles or posterior fossa malformation can be detected in the first trimester of pregnancy, but requires a detailed ultrasound evaluation an increase skill level of the sonographer and appropriate high-tech equipment.

At 11-14 weeks, three spaces can be measured in the posterior brain of the fetus by using the mid-sagittal view of the fetal face when assessing the nuchal translucency: the brainstem (BS), the fourth ventricle (IT) and the cisterna magna (CM).

There is a strong correlation already proved between a decreased amount of fluid in the posterior brain and open spina bifida.

Recent research suggests that cystic posterior fossa anomalies like Dandy Walker malformation (DWM) and Blake's pouch cyst may be hinted by increased fluid in the posterior brain [3].

Material and Methods

We analyzed the results of a one year of first trimester examinations in the prenatal diagnosis department within the University Hospital of Craiova, part of a PhD study that included a special study of the fetal CNS that targeted a series of standard sections and certain signs in order to optimize first trimester diagnosis.

All patients were examined by using transabdominal and transvaginal approach by using a Voluson E8 Expert (GE Medical Systems, Zipf, Austria) with a RAB-6D, and RIC5-9-D transducers.

All patients were informed regarding the research project, enrollment in the study being done only after appropriate notification and written consent obtaining of the patient in agreement with Commission of University and Scientific Ethics and Deontology of University of Medicine and Pharmacy of Craiova.

The fetal CNS anatomy assessment was based on a pre-established protocol which included specific anatomic landmarks.

We assessed each fetus by using the axial planes and mid-sagittal view of the fetal face

and brain according to The Fetal Medicine Foundation (FMF) [4] recommendations.

In all cases we measured the crown-rump-length (CRL), the nuchal translucency (NT), the intracranial translucency (IT), and we assessed the fetal nasal bone, the tricuspid valve flow and the ductus venosus.

In addition, we analyzed the shape of the fetal head and structures such as the thalamus and the posterior fossa.

At the level of the posterior fossa we identified: the brainstem, the fourth ventricle also called the intracranial translucency and its choroid plexus, the cisterna magna, an anechoic structure placed behind the fourth ventricle and in front of the occipital bone.

Supplementary, in the mid-sagittal plane we assessed the following markers for the first trimester diagnosis of spina bifida and posterior fossa anomalies: "the octopus sign" described by Elena Andreeva (Moscow, 2013) [5] and the BS/BSOB (brainstem/brainstem-occipital bone) ratio, a marker described by Lachman and Chaoui [6] (Fig.1).

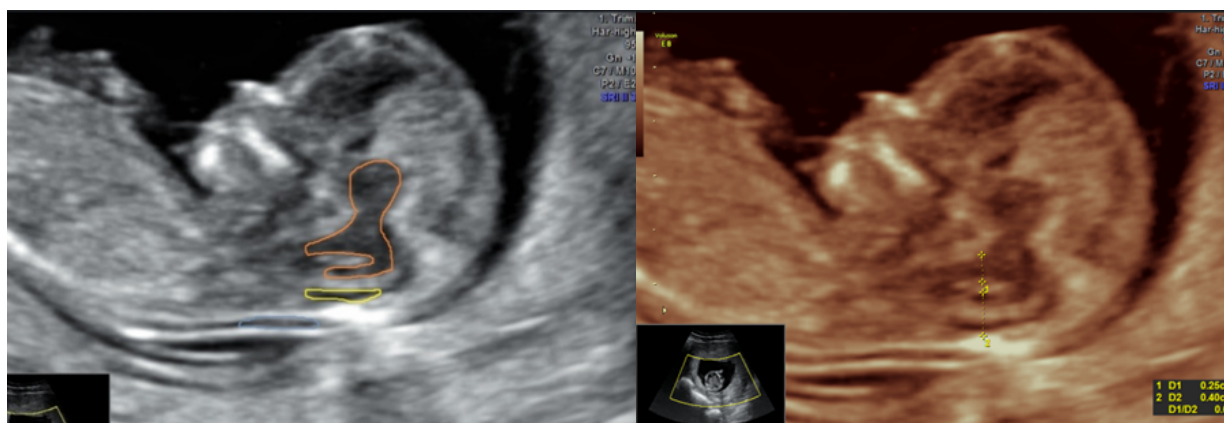


Fig.1. The octopus sign. 2. BS/BSOB ratio-normal findings

The octopus sign was assessed in order to detect its value in the diagnosis of spina bifida and Dandy Walker malformation in the first trimester of pregnancy. The normal octopus sign diagram looks like that [5]:

- Both arms of the octopus have almost similar measurements.
- The two arms can be visualized separately- the first arm represented by the brainstem and the second one represented by the fourth ventricle with its choroid plexus.
- The cisterna magna is visualized distinctively from the second arm of the octopus.

The octopus sign was evaluated after its appearance and it was considered normal or abnormal in compliance with the case.

In case of spina bifida, there is an increasing in size of the first arm of the octopus, a decreasing of the second arm, and cisterna magna cannot be visualized, while in case of posterior fossa anomalies, the second arm of the octopus increases and the first arm decreases in size.

Regarding the BS/BSOB ratio, we measured the thickness of the brainstem and its distance to the occiput. We opted for a cut-off of 1 according with the results obtained by

Lachman and Chaoui in their research in 2011 [6].

The fetal brain was also assessed in four axial planes by following certain anatomical landmarks according with the recommendation of Chaoui and Abuhamad [7]. The four planes used were:

1. The axial plane at the level of the lateral ventricles;
2. The axial planes at the level of the thalamus;
3. The axial-oblique plane at the level of the posterior fossa.
4. The axial planes at the level of the orbits.

In the first 3 planes we assessed the shape of the fetal head and its integrity, the ossification of the fetal head bones, the falx cerebri, and the aspect of the cavum septum pellucidum (CSP). In the transventricular plane, we identified the two choroid plexi of the lateral ventricles, in the transthalamic plane, the two separated thalamic masses, aspect of the CSP, of the cerebral peduncles and the cerebral aqueduct. By using the fourth plane, we tried to visualize the fetal cerebellum but only with transvaginal approach. We also tried to detect the hourglass shape fourth ventricle with its choroid plexus and the future cisterna magna. The orbits containing the two eyeballs and the nose in the midline were assessed in the fourth plane.

In the transventricular plane, we assessed the CP/HA ratio (the ratio between the area of the two choroid plexi and the area of the fetal head) in 2D and 3D examination. The area of each plexus was obtained by using the "area trace" mode and the area of the fetal head by using the "ellipse" mode. The sum of the area of each choroid plexus was divided by the area of the fetal head. We decided a cut-off of 0,36 according to a study conducted in our unit by our team in 2016.

This marker showed promising results especially in the planes obtained after volume processing, situation that assures the accuracy of the transthalamic planes (in this way the oblique planes that decrease the accuracy and increase intra and interobserver discordances are avoided).

Maternal biochemistry (free β HCG and PAPP-A) was documented and the estimated risk for chromosomal disorders was calculated using the FMF software. Whenever suspicious, we recommended invasive tests or in some cases noninvasive tests-NIPT after a thorough genetic counselling.

Results

Over a one-year period, the study included 1376 patients. The pathologies diagnosed were (Table 1).

Table 1. The anomalies encountered during the one-year research

DIAGNOSIS	NUMBER OF CASES
Acrania	1
Holoprosencephaly	1
Dandy Walker syndrome	1
Spina bifida	3

Acrania

During our study, we detected one case of acrania at 12 weeks and 6 days of amenorrhoea. The CRL measured at the moment of the detection was 62,57mm corresponding to a 12 weeks and 4 days pregnancy. The diagnosis was based on an irregular shape of the fetal head, the absence of the calvaria with the presence of an abnormal tissue at the level of the fetal head with the typical appearance of the "Mickey Mouse" and "frog eyes" signs (Fig.2). The couple was counseled regarding the poor prognosis and decided to terminate the pregnancy without genetic evaluation of the karyotype from the abortion product due to personal reasons.



Fig.2. Acrania-sonographic aspects

Holoprosencephaly

We also detected one case of fetal alobar holoprosencephaly in a singleton pregnancy in a 65,1mm fetus, corresponding to a 12w6d of pregnancy. The diagnosis was attested on axial plane and the absence of the butterfly-shape choroid plexus of the lateral ventricles was highly suggestive for the diagnosis. After proper counselling, the couple opted for termination of pregnancy (TOP). The genetic assessment from the postabortum product revealed a Trisomy 13 Karyotype (Fig.3, Table 2).

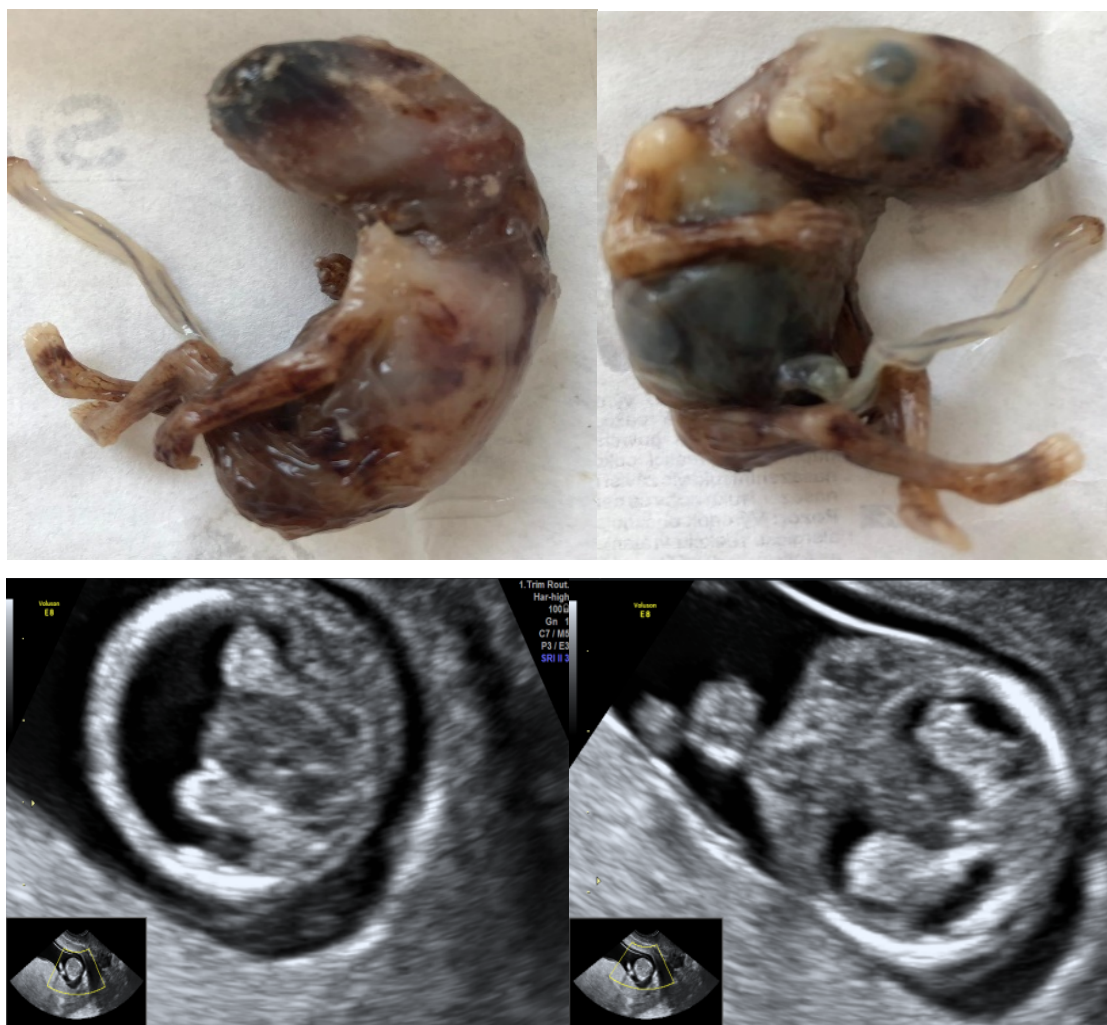


Fig.3. Holoprosencephaly-sonographic and pathological aspects

Table 2. Specific features of the case of holoprosencephaly

SUMMARISATION OF THE CASE OF HOLOPROSENCEPHALY	
Gestational age	12w6d
CRL	65,1 mm
Karyotype	Trisomy 13

Spina Bifida

Within the study we detected in the one-year period 3 cases of open spina bifida. All three cases were detected at 11-14 weeks assessment.

The abnormal appearance of the fourth ventricle in the mid-sagittal view of the fetal head was highly suspicious for the diagnosis. We measured in all patients the BS/BSOB ratio and the CP/HA ratio and assessed the octopus sign in all patients evaluated during the research. The couples chose TOP in all cases. The karyotypes were normal in two cases. In the third case, we could not obtain information regarding the karyotype due to the fact that the patient lost the pregnancy spontaneously and was treated in another hospital (Table 3, Fig.4).

Table 3. Specific features of the cases with spina bifida

Features	1	2	3
CRL	52,6	69,8	75,9
OUTCOME	TOP	TOP	Misscariage
KARYOTYPE	Normal	Normal	Unavailable
IT	Abnormal	Abnormal	Abnormal
BS/BSOB	1,74	2,12	1,82
CP/HA	0,410	0,389	0,378
Octopus sign	Abnormal	Abnormal	Abnormal

All the markers assessed showed abnormal features in pathological cases

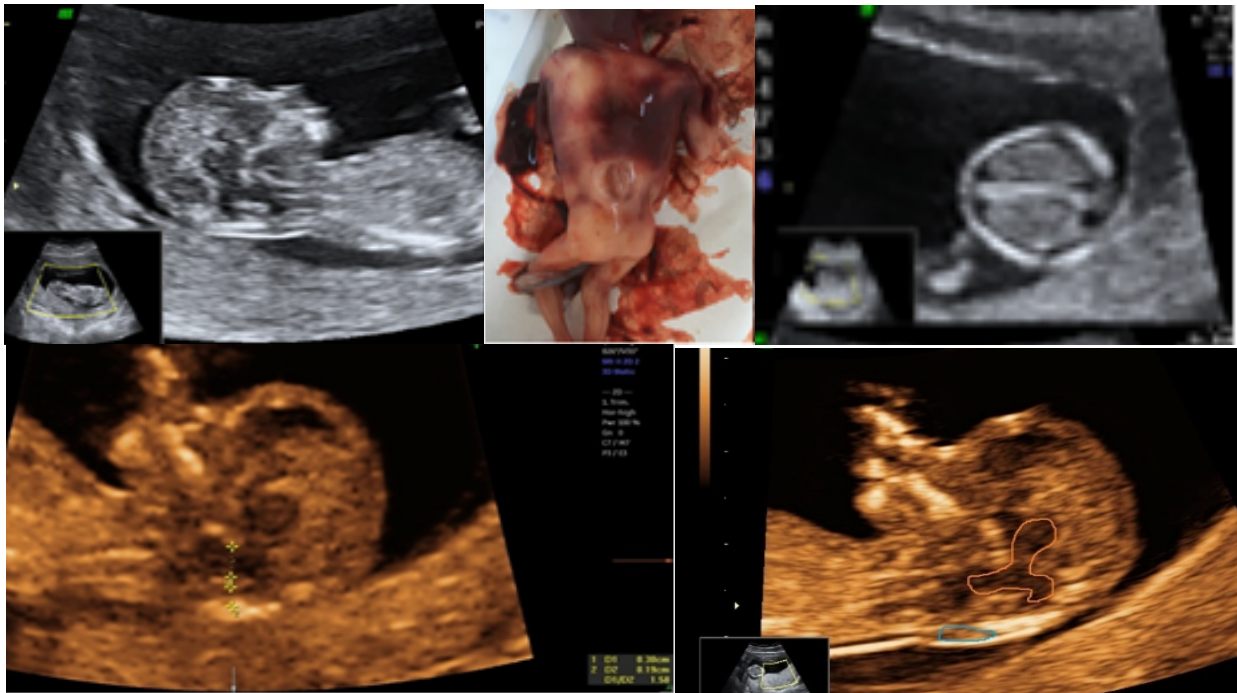


Fig.4. Spina bifida-sonographic appearance

Dandy Walker Malformation

During our research we suspected a case of Dandy Walker malformation (DWM) in the first trimester of pregnancy (Table 4). The diagnosis was attested by the abnormal increase intracranial translucency, a small brainstem and an inappropriate image of the choroid plexi of the fourth ventricle. Also, by using the axial views we could highlight the cystic transformation of the posterior fossa. The octopus sign showed an abnormal appearance in the assessment of the mid-sagittal view of the fetal brain (Fig.5).

Still, reevaluation at 18 weeks ascertained the diagnosis. The couple opted for termination of pregnancy and refused genetic assessment of the abortion product.

Table 4. Specific features of the case with DWM

Gestational age	12w6d
CRL	65,8 mm
IT	Abnormal
Octopus sign	Abnormal
Karyotype	Unavailable
Outcome	TOP at 18w

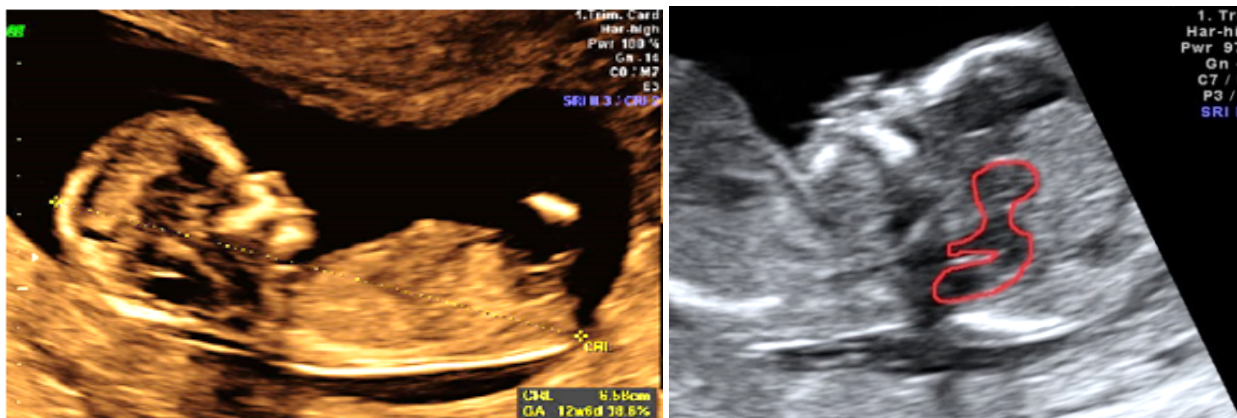


Fig.5. Dandy Walker malformation-sonographic findings in the first trimester of pregnancy

Discussion

As we expected the first trimester ultrasound assessment of the fetal brain allowed the detection of major anomalies with debilitating or life threatening effect.

At 11-14 weeks, most of the cases we confronted with were neural tube defects (one case of acrania and three cases of open spina bifida).

According with the specialty literature, detection of these kind of anomalies have become routine at 11-14 weeks of gestation, but cases of acrania are stated to be detected as early as 8-10 weeks of gestation in some situations [8,9].

In the late years, general interest was lowering as much as possible the gestational age of detection of malformations like neural tube defects or even posterior fossa anomalies.

In concordance with the actual tendency, we tried to use innovative methods to increase the diagnostic accuracy of the first trimester ultrasound.

Since 2009, when R. Chaoui described the "intracranial translucency" [10] as a new marker for open spina bifida detection, there was a focus in the screening for spina bifida from the second trimester (where aspects like banana sign or lemon sign established the diagnosis) to the first trimester of pregnancy.

In agreement with the data from the literature, we tried to use innovative markers in order to optimize the detection of this kind of anomaly in the first trimester of pregnancy.

By corroboration of most of the markers described by the literature so far (intracranial translucency, octopus sign, BS/BSOB ratio)-and by adding a new marker discovered by our team in our department (CP/HA), we managed to detect all cases of spina bifida referred to our unit during a one-year period.

New studies describe new diagnostic markers for the antenatal detection of spina bifida such as the biparietal diameter [11] and cisterna magna size [12].

In her research, Khalil noticed a decrease of the biparietal diameter size under the 5th percentile in 44% of the fetuses with spina bifida assessed at 11-14 weeks [11].

Although carried out on a narrow lot of 5 cases, the study of Garcia-Posada describes as a very valuable marker for the detection of spina bifida, a cisterna magna size under the 5th percentile [12].

All the detection methods have a common feature-all of them are focused on the assessment of the fetal head with the identification of some indirect signs and not on the highlighting of the defect at the level of the spine.

We also detected a case of alobar holoprosencephaly during our research. The anomaly was detected at 12w6d.

In spite of the fact that most of the cases with fetal holoprosencephaly are diagnosed at the 11-14 weeks scan, Blaas states cases of holoprosencephaly detected at 9w2d of gestation [13].

Our case occurred in the context of a chromosomal disorder-Trisomy 13.

The literature shows a strong correlation between fetal holoprosencephaly and trisomy 13 and 18 [14].

Regarding the case of Dandy Walker Malformation, the diagnosis was established only at 18 weeks.

The literature states that most of the cases of fetal DWM are detected after 17 weeks of gestation [15], since at 11-14 weeks the assessment of the posterior fossa can lead to a high incidence of false-positive diagnosis [7,15].

Still, the detection of an abnormal appearance of the posterior fossa at 11-14 weeks can highlight the need of a detailed assessment later in pregnancy as most of them are associated with fetal posterior fossa malformations in the second trimester of pregnancy.

In all pathological cases the markers assessed were abnormal with no false negative results.

Consequently, the evaluation of as many as possible markers of diagnosis increases the detection rates of fetal CNS anomalies.

Still, the need of larger study populations is compulsory for a proper statistical processing.

Conclusion

In conclusion a detailed sonogram at 11-14 weeks of pregnancy is feasible.

Nowadays, the first trimester ultrasound assessment is able to detect anomalies such as neural tube defects, holoprosencephaly and can draw attention regarding subtle findings for the diagnosis of posterior fossa anomalies.

The detection of these anomalies at such early age offer the possibility to legally terminate the pregnancy in safe conditions with low negative obstetrical, psychological and financial side effects.

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*Corresponding Authors: Elena Mădălina Barbu, PhD Researcher,
University of Medicine and Pharmacy of Craiova, St. Petru Rares No. 2, Craiova 200349, Dolj, Romania,
e-mail: cmibarbu@yahoo.com;
Alexandru Cristian Comanescu, Department of Obstetrics and Gynecology,
University of Medicine and Pharmacy of Craiova, St. Petru Rares No. 2, Craiova 200349, Dolj, Romania,
e-mail: alexcom8000@gmail.com*