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Evaluation Of 2D Versus 4D Ultrasonography On Midline Structures Of The Fetal Brain In The Second

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Abstract
Background: *Midline brain structures are critical for normal morphogenesis and function of the fetal brain. However, it is a diagnosis of congenital anomaly of midline brain structures.*
Job Objectives: *This study aims to evaluate the role of 2D versus 4D ultrasound in the diagnosis of midline structures of the fetal brain in the second trimester of pregnancy.*
Patients and methods: *200 pregnant women in the second trimester [18–22 weeks] were selected. They are evaluated clinically to check the well-being of the woman and fetus. Then an examination of the midline stricture of the fetal brain is carried out using two- and four-dimensional ultrasound, which aims to find any abnormalities in the midline structure of the fetal brain. Both scans were compared with postnatal transcranial ultrasound.*
Results: *2D ultrasound did not detect abnormalities in 194 of 200 fetuses [97.0%], and 4 cases [2.0%] had mega-cisterna magna, and 2 cases [1.0%] had encephalomylocele, which was detected by 4D and confirmed by postnatal transcranial ultrasound. 4D ultrasound found 2 cases [1.0%] of Dandywalker malformation, which were confirmed by postnatal transcranial ultrasound. There was complete agreement between prenatal 4D ultrasound and postnatal transcranial ultrasound. Prenatal 2D ultrasound had a sensitivity of 75.0%, specificity of 100.0%, PPV of 100.0%, NPV of 98.7% and overall accuracy of 99.0%. Otherwise, prenatal 4D ultrasound is 100.0% sensitive and specific.*
Conclusion: *4D ultrasound shows superiority in the diagnosis and confirmation of fetal brain midline structural abnormalities. Additionally, prenatal 4D ultrasound was 100.0% sensitive compared to postnatal transcranial ultrasound.*
Keywords: *Two Dimensions; Four Dimensions; Midline Structure of the Fetal Brain; After birth; Transcranial Ultrasound.*

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I. Introduction

malformation and concluded that, this instrument can be used as a complementary instrument in assessment. Fetal malformations are associated with an increased risk of newborn defects. If fetal malformations are diagnosed early in pregnancy, it is worth making a decision whether to terminate the pregnancy or not. Therefore, regular pregnancy checks are the key to reducing the rate of newborn defects [1]. Reducing defective fetuses will improve the quality of newborns and encourage the development of society and families. Therefore, antenatal examination is very useful for congenital malformations of the fetus, especially congenital anomalies of the face, spine, extremities and abdominal wall. In fetuses at high risk of CNS malformation or in suspicious cases, basic examination requires a fetal neurosonogram, which should be performed by an expert investigator.[6].To assess satisfactory visualization of the median structures, classical examination should be used in combination with modern techniques[18].

Organogenesis of the central nervous system from the neural tube begins early in intrauterine life, and goes through a series of differentiation processes until after birth.[3]. The neural elements contained in the midline brain structures are essential for normal morphogenesis and brain function so median echo should be assessed at the end of the first trimester [4]. Diagnosis of congenital brain anomalies includes structure

II. Research Purposes

This study was conducted to investigate the efficiency and accuracy of two-dimensional versus four-dimensional ultrasound in diagnosing midline structures of the fetal brain in the second trimester of pregnancy [18–22 weeks] confirmed by postnatal transcranial examination. Ultrasound. Midline abnormalities are difficult to perform during fetal life because routinely used standard axial sonography does not show some brain structures such as the cerebellar vermis and corpus colossum.[5]. However, in high-risk pregnancies during the first to early second trimester, midline abnormalities can be seen.[6]. The classification of midline anomalies was first reported

by De Meyer and later revised by Fitz et al. includes two main classes: closure defects and diverticulation disorders[7, 8]. Cerebral midline ontogenesis occurs after the seventh week of amenorrhea which is known as ventral initiation which is closely related to the development of the midface.[9].

III. Patients And Methods

After obtaining ethical approval from the ethics committee of the Department of Obstetrics and Gynecology, Damietta Medical Faculty, and Assiut Medical Faculty, Al-Azhar University, written consent was signed by each participant. The current work was completed by 200 pregnant women during the second trimester [18–22 weeks of gestation]. This study was completed between January 2019 and June 2021. All pregnant women in the second trimester, normal and high-risk pregnancies [diabetes, hypertension, heart disease, smoking, drinking alcohol, and using illegal drugs] and subjects who had children with routine ultrasound examinations were included. an established antenatal care tool as it is a simple noninvasive method that is essential in routine prenatal assessment, and is a starting point in neuroscience studies[10, 11]as well as increasing the detection rate of fetal brain malformations[12].

Congenital brain abnormalities. anomalies were registered in this study. Any women who refused to participate, in the first and third trimesters of pregnancy, who had twin or multiple pregnancies as well as intrauterine fetal death, were excluded from the study.

The use of a detailed morphological ultrasound protocol allows an increase in the first trimester detection rate of 69.5% of major CNS malformations[13].Visentindkk. reported their experience in the use of transfrontal viewing as a new two-dimensional [2D] method for imaging fetal midline brain structures and facial profiles.[14].

All women were evaluated with clinical history and examination. Ultrasound evaluation of fetal midline structures was completed with the VoLuSON p5 device. A 2.0–5.0 MHz Curved Linear Array probe was used for 2D imaging, and a 2–6 MHz broadband volume curved ultrasonic transducer was used for 4D imaging. In each case, effortperformed to obtain the median plane of the fetal brain with two-dimensional [2D] ultrasonography followed by four-dimensional [4D] ultrasonography in the same session. The transducer is aligned with the anterior fontanel and midline suture via a transvaginal approach [according to International Society of Ultrasound in Obstetrics and Gynecology guidelines] or by transabdominal scanning when transvaginal scanning is technically difficult, or to obtain a good image. All parts of the fetus are assessed, starting with the fetal skull, and the findings are recorded. Visualization of relevant anatomical details in the median plane, particularly the corpus callosum and cerebellar vermis, was recorded for 2D and 4D images. An attempt was made to visualize the main landmarks of the cerebellar vermis, namely the fastigium of the fourth ventricle and the two main fissures. 2D images were first acquired with a wideband volume curved probe. Then, a 4D volume image is obtained after creating a field box that is fitted to the desired area. The 2 and 4D images are placed side by side on the screen and the 4D image is acquired in full screen. Volume data were acquired with the 4D real-time option, provided that the acquisition time was <20 seconds per film volume, and the scanning angle ranged from 30° to 60°. Of the 4D-ultrasound imaging modalities, only surface rendering mode [SRM] was used. The average duration of each examination is 25 minutes [20-30 minutes]. However, no time limit is set before an anomaly scan. Cephalocele is defined as a neural tube defect characterized by protrusion of intracranial structures [brain tissue] through a defect in the skull. On axial view, this lesion is recognized as a brain-associated cranial cystic lesion (Figure 1). On the other hand, Mega cisterna magna is characterized by enlargement of the retro and infracerebellar CSF spaces [the space between the inferior margin of the vermis and the posterior edge of the foramen magnum] [Figure 2].

(Figure 1 Axial View Of The Fetal Brain Showing A Cranial Cystic Lesion Confirmed By 4D And Postnatal Transcranial Ultrasound)

(Figure 2 Transcerebellar Axial Fetus Showing Mega Cisterna Magna.)

After birth Transcranial ultrasound was performed for all newborns and was used as a reference tool to ensure the diagnostic efficiency of 2D and 4D ultrasound.

Statistical analysis: Data were anonymized and entered into Microsoft Excel, version 2016 [Microsoft Inc., USA]. Percentages were calculated for categorical data and diagnostic indicators for each modality were calculated manually from the following equations.

- Sensitivity = true positive [TP]/[true positive + false negative [FN]].
- Specificity = true negative [TN]/[true negative + false positive [FP]].
- Positive predictive value [PPV] = TP/[TP+FP].
- Negative Predictive Value [NPV] = TN/[TN+FN];
- Overall Accuracy=TP+TN/TP+TN+FP+FN

IV. Results

The age of the study group ranged from 18-41 years and was distributed as 20% of women were less than 20 years old, 64% of women were between 20-30 years old and only 16% were more than 30 years old. Gestational age ranged from 18-22 weeks with a mean of 20 weeks. In the current study, 2D ultrasound detected no abnormalities in 194 of 200 fetuses [97.0%], and 4 cases [2.0%] had mega-cisterna magna, which was detected by 4 D and confirmed by postnatal transcranial ultrasound. in addition, 2D USG detected 2 cases [1.0%] suffering from encephalomylocele, which was found and related to the brain [most likely encephalocele] On the other hand, 2D USG did not find any cases of Dandywalker malformation, but 4D USG found 2 cases [1.0%] confirmed by postnatal transcranial US. There was complete agreement between prenatal 4D ultrasound and postnatal transcranial ultrasound [Table 1]. Using postnatal transcranial ultrasound as the reference standard, prenatal 2D ultrasound had a sensitivity of 75.0%, specificity of 100.0%, PPV of 100.0%, NPV of 98.7% and overall accuracy of 99.0%. Otherwise, prenatal 4D ultrasound was 100.0% sensitive and specific [Table 2].

Table 1. Diagnosis of anomalies detected among the studied population with different diagnostic modalities

Detected anomaly	2D [n=200]	4D [n=200]	Ultrasoundpostnatal transcranial [n=200]
NAD	**194 [97.0%]**	**192 [96.0%]**	**192 [96.0%]**
Mega-cisterna Magna	**4 [2.0%]**	**4 [2.0%]**	**4 [2.0%]**
Encephalomylocele	**2 [1.0%]**	**2 [1.0%]**	**2 [1.0%]**
Dandywalker Malformation	-	**2[1.0%]**	**2[1.0%]**

Table 2. Sensitivity and specificity of 2D and 4D for the detection of fetal brain midline abnormalities using the postnatal transcranial ultrasound method as the reference standard

Two-dimensional ultrasound		**Four-dimensional ultrasound**
Really positive[etc]	6	8
False positive[FP]	0	0
Totally negative[TN]	192	192
False negative[FN]	2	0
Sensitivity	75.0%	100.0%
Specificity	100.0%	100.0%
Positive predictive value[PPV]	100.0%	100.0%
Negative predictive value[NPV]	98.7%	100.0%
Overall accuracy	99.0%	100.0%

Sensitivity = TP/TP+FN; Specificity = TN/TN+FP; PPV: = TP/[TP+FP]; NPV: = TN/[TN+FN]; Accuracy=TP+TN/TP+TN+FP+FN comparing prenatal ultrasound with magnetic resonance

V. Discussion

Fetal malformations are usually caused by genetic abnormalities. This can be stimulated by exposure to drugs in the womb (eg tetracycline and streptomycin), radiation, smoking, and alcohol intake [19]. Currently, two-dimensional ultrasound is a screening method imaging [MRI] and reported that ultrasound was unable to find prenatal CNS abnormalities in 72.2% and had a specificity of 100.0%. They concluded that ultrasound is a relatively accurate, safe and relatively inexpensive tool for screening CNS malformations in the prenatal period. However, they use 2D and 3D ultrasound modalities.

However, it has certain limitations [e.g. artifacts and low image resolution] that reduce its diagnostic accuracy [20]. With advances in technology, three- and four-dimensional ultrasound were introduced and play an additional role to 2D ultrasound, and can stand alone as effective diagnostic tools[21]. Here, we go one step further and include 4D ultrasound, and instead of prenatal MRI, we use postnatal transcranial ultrasound to minimize the risk of radiation exposure to the fetus and mother. In addition, we carry out examinations in the second trimester of pregnancy [gestational age 18-22 weeks] as recommended by obstetric guidelines for antenatal care to examine fetal anatomy.

In the current study, 2D showed no abnormalities in 97.0% of the population studied compared to 96% found with 4D ultrasound. Detected midline abnormalities by this time, the major and midline intracranial structures have been established and can be traced by sonographic visualization [6]. were 3.0% and 4.0% with two- and four-dimensional ultrasound, respectively. Abnormalities detected with four-dimensional ultrasound are identical to postnatal diagnoses with transcranial ultrasound. The reported incidence rate of fetal midline cerebral abnormalities is within the incidence rates reported in previous literature. For example, Milanidkk.[6] reported that fetal central nervous system [CNS] abnormalities are quite common. The incidence rate ranges from 0.1 to 0.2% in live births and increases to 3-6% in stillbirths. In terms of frequency, fetal CNS abnormalities occur after cardiac abnormalities. Wang et al.[25] used 2D and 4D to estimate the diagnostic value of fetal craniocerebral malformations. They reported that, the accuracy of 4D alone was significantly higher than 2D and the accuracy of the combined approach [2D plus 4D] was better than each modality alone. The two methods are identical with the actual diagnosis of 96.05% of all anomalies, while 4 D is sensitive at 82.89% and 2 D sensitivity is 69.74%. Of note, all patients included in their study were known to have abnormalities before their examination and evaluation was performed

Prenatal ultrasound is a non-invasive, simple, readily available and cost-effective tool for prenatal screening. Thus, it could be an effective imaging modality for screening fetal brain abnormalities, as reported by Onkardkk.[22] and Tutus et al.[23]. Goncalvesdkk.[24] retrospectively.

4D ultrasound can provide multi-layered images in real-time because it scans organs from multiple angles. In this way, the fine structures of the fetus can be examined directly and clearly. With 4D ultrasound, accurate differential diagnosis of various brain lesions can be achieved through observation specificity of 3D/4D ultrasound was 92.2% and 76.4%, respectively

In this study, 2D ultrasound failed to detect Dandywalker malformation. However, 4D can detect it and the diagnosis is confirmed correctly via transcranial ultrasound and 2D ultrasound were 96.1% and 72.7% but there was no significant difference [22]. postnatal. Korea et al.[27] described it as the most common congenital cerebellar malformation, with hypoplasia or agenesis of the cerebellar vermis with enlargement of the posterior fossa, ventriculomegaly, and dilation of the fourth ventricle. This abnormality can be detected with prenatal ultrasound. however, other abnormalities include cranial displacement of the tentorium, torcula, and lateral venous sinuses that can be seen with prenatal MRI. Bosemani et al.[28] reported that prenatal posterior fossa ultrasound is a challenging task from a technical point of view. Agenesis of the vermis with cephalad rotation of the remaining cerebellar vermian is best seen in the sagittal plane. In the axial plane, artifactual vermian gaps can occur due to excessively steep angulation, leading to a false-positive diagnosis. In addition, there are other abnormalities that resemble dilatation of the cisterna magna [for example mega cisterna magna and posterior fossa arachnoid cyst].

On the other hand, Mittermayer et al.[35] reported that, although 2D and 4D ultrasound are able to detect various types of fetal brain malformations, several studies show that the detection rate of fetal brain anomalies with 2D and 4D ultrasound is only around 40-50%.

The current study had a unique prospective design, namely screening for malformations in the entire group of pregnant women. However, one of the limiting measures is the small number of women involved in screening which results in a low number of malformations. In addition, there are many challenges facing the implementation of prenatal screening with ultrasound. These include maternal obesity, fetal position, echo antifixation and oligohydramnios which can limit the capabilities of ultrasound and reduce its image resolution. Early ossification of the fetal skull is another challenge[36, 37]. Therefore, magnetic resonance imaging (MRI) has been practiced, with the advantage of better resolution of soft tissue contrast, planes

Dandy-Walker malformation can be isolated or associated with other genetic abnormalities and its prognosis depends largely on the degree of ventriculomegaly, requiring follow-up with prenatal ultrasound and

postnatal MRI for greater visibility, and the opportunity to obtain multiplane images makes fetal MRI an important diagnostic tool .[38].

Predict the severity of neurodevelopmental delay.[29]. In line with his current work, Glenn et al.[30] reported that, fetuses with Dandy-Walker malformation can have normal intellectual function, especially with normal vermis lobulation and no additional fetal brain abnormalities.

On the other hand, MRI image quality may be negatively affected by fetal movement during scanning, which may limit the diagnostic accuracy of MRI in some cases. Therefore, ultrafast MRI has been introduced to reduce the adverse effects of fetal movement[39, 40]. Therefore, the use of 4D ultrasound which considers fetal movements as an MRI

Early diagnosis of Dandy-Walker syndrome is useful for predicting prognosis and planning delivery[29]. ultrafast and free from high costs and exposure to radiation risks, adding value to this research.

In this study, the diagnosis of mega cisterna magna and encephalomylocele was carried out using 2D and 4D ultrasound. Hamisadkk.[31]found that the giant cisterna magna was diagnosed in three cases using 2D and 4D ultrasound during the prenatal period and this was confirmed by postnatal MRI. As for encephaloceles, prenatal 2D ultrasound detects approximately 80% of encephaloceles[32]. In another study, 4D US and MRI confirmed the diagnosis of encephalocele more than It can be concluded that 2D US still plays a role in the diagnosis of fetal brain midline abnormalities. 4D ultrasound demonstrated superiority in the diagnosis and confirmation of midline structural abnormalities, and correlated completely with postnatal transcranial US diagnosis. However, further evaluation of the accuracy and efficiency of 4D in the diagnosis of midline structural anomalies should be investigated in large population 2D studies[33].

Focus location, size and structure, spatial relationship with the surrounding parenchyma, and image stability with fetal movement [26]. diagnosed by 2D ultrasonography showed concordance with 3D/4D in 90.4% of findings. When compared with the diagnosis made after delivery, the sensitivity and This study shows that, the sensitivity of 4D versus 2D is 100% versus 75.0%, the specificity and positive predictive value are 100% in 2D and 4D while the negative predictive value is 100% in 4D and 98.7% on 2D US. 4D accuracy is 100% compared to 99% for US 2D. In Gonçalvesdkk's study.[34]

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