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Comparative Study between The Role of Two dimensional and Three Dimensional Ultrasound in Assessment of Fetal Central Nervous System Congenital Anomalies

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ABSTRACT

Background: Three dimensional ultrasound (3D US) has become the new standard in prenatal diagnosis of fetal congenital anomalies. This technique enables detailed examination of the fetal anatomy and higher quality depiction of congenital anomalies. Furthermore, four dimensional ultrasound (4D US) enables visualization of more details regarding the dynamics of small anatomical structures. Using the advantages of this technology, a physiologic pattern of embryonic or fetal motor development was made.

Objective: This study aimed to evaluate the role of three dimensional (3D) ultrasound compared with two dimensional (2D) ultrasound in diagnosis of fetal central nervous system congenital malformations.

Patients and Methods: This Prospective study was performed on total 100 patients with gestational age from 18 weeks to 24 weeks who underwent 2D ultrasound then examined by 3D ultrasound at Obstetrics and Gynecology Department, Bab el-Sheria, Al-Azhar University Hospital.

Results: Statistical analysis revealed that the most common neurological malformations detected were Holoprosencephaly and Anencephaly which had significant high agreement between 2D and 3D regarding their diagnosis. There was significant agreement between 2D and 3D regarding the congenital fetal spinal and cranial malformations. The 2D and 3D ultrasound provided equal diagnostic information in microcephaly while 3D US provided more diagnostic information than 2D US for Choroid plexus cyst, agenesis of the corpus callosum and spina bifida.

Conclusion: In comparison with 2D US, 3D US improves the diagnostic capability by illustrating more diagnostic details in evaluation of malformations of the fetus, especially in visualization of fetal malformations of the small cranial anomalies and spina bifida.

Keywords: *Fetal; Central Nervous System; Congenital Anomalies; Two dimensional; Three dimensional Ultrasound.*

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INTRODUCTION

Fetal congenital anomalies risk is reported to be about 2% to 3% regardless of their prior history, family history, maternal age or lifestyle. This risk increases in some patients (high risk pregnancy). Among these factors that increase the risk of fetal congenital anomalies are advanced maternal age, history of drug intake (teratogenic drugs) during first trimester, maternal smoking & alcoholism, exposure to radiation, prior history of recurrent abortion or delivery of malformed fetus . [7]

Congenital deformities represent 20-25% of perinatal demises. Presently, numerous hereditary and different issues can be diagnosed early in pregnancy. Antenatal diagnosis utilizes different non-invasive and invasive procedures to decide the wellbeing of the condition or any anomaly in an unborn fetus . [1]

The neural system malformation is one of common congenital anomalies encountered in pregnancy. [16]

They represent about 0.3-1 % of all live births. During prenatal anomaly scan, detection of CNS malformation is important especially these anomalies have a poor prognosis and also associated with genetic syndromes or chromosomal anomalies. [15]

The CNS development start from 3 weeks to 20 weeks of intrauterine fetal life. Often all neural anomalies are a result from defect in embryogenesis at certain points of development. Ultrasongraphy can detect many CNS anomalies in the first and an early second trimester. Some of them develop or become obvious at end of pregnancy. The earlier in detection, the more time available for the parents and clinician to plan the outcome of pregnancy. Extensive and severe life threating disorders give reason for early

termination of pregnancy, and detection of minor disorders helps everybody to be prepared and reassured for post-delivery management. [4]

Two dimensional (2D) ultrasonography, antenatal detection of many types of central nervous system anomalies have been detected. 2D sonography can diagnose many fetal abnormalities. Due to defects in third dimension, some of them cannot be seen with the conventional technique, this depend on the defect type and the limitations of fetal position. [10]

Three dimensional ultrasound (3DUS) has become the new good standard in intrauterine diagnosis of fetal congenital anomalies. This technique allowing fetal anatomical examination in details and higher quality illusteration of congenital anomalies. Dynamics of the small anatomical structures can be visualized in more details via four dimensional ultrasound (4D US). The advantages of this technology can be used in assesment of an embryonic physiological pattern or fetal motor development. [17]

The aim of this study is to evaluate the role of three dimensional (3D) ultrasound compared with two dimensional (2D) ultrasound in diagnosis of fetal central nervous system congenital malformations.

PATIENTS AND METHODS

This prospective study which was performed at Obstetrics and Gynecology Department, Al-azhar University Hospital included 100 patients with gestational age from 18 weeks to 24 weeks by 2D ultrasound then examined by 3D ultrasound with the following criteria:

Inclusion criteria included Age of 18 to 40 years old pregnant women and pregnant women Suspected to have fetal CNS malformations during routine antenatal obstetric evaluation.

Exclusion criteria included Women with no suspected fetal neurological anomalies.

This study was conducted regarding ethical committee Faculty of medicine, Al-Azhar University after informed consent was taken from all cases after complete demonstration of the study purpose before rolling in this study**.**

Initially, traditional 2DUS was routinely performed. Assessment of fetus include (The heart, thorax, abdominal wall, abdominal viscera, limbs, spines, head and neck).

After complete examination by the 2D sonography, initial diagnosis was done based on the detected findings. After intial diagnosis, patients were undergoing evaluation by 3DUS to obtain data by 3D imaging compared to the 2D findings, and if the 3D imaging displayed any superiority in diagnosis.

A 3D US volume was taken to scan all regions, as well as the area of interest when 2DUS detected pictures with various filter settings was used to differentiate between the soft tissue & bony features. The 3D images was compared with the 2D images. The results obtained with 2D and 3D US was compared according to identification, localization, size and depth of the malformation detected.

Ethical Considerations: The patient data were anonymous. Data presentation was not be by the patient name but by diagnosis and patient confidentiality was protected. Study protocol was submitted for approval by ethics committee of Faculty of Medicine - AL Azhar University.

Statistical analysis:

The collected data were coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 22.0, IBM Corp., Chicago, USA, 2013. Quantitative normally distributed data described as mean±SD (standard deviation) after testing for normality using Shapiro-Wilk test, then compared using independent t-test if normally distributed and Mann Whitney test if not normally distributed, while Pearson test was used for correlations. Qualitative data described as number and percentage and compared using Chi square test and Fisher's exact test for variables with small expected numbers. Log rank test was used to compare abortion rate. The level of significance was taken at P value < 0.050 was significant, otherwise was non-significant.

RESULTS

The most frequent neurological malformations were Holoprosencephaly and Anencephaly (**Table 1)**.

Diagnosis	3D	2D
Normal	12 (12.0%)	17 (17.0%)
Holoprosencephaly	14 (14.0%)	13 (13.0%)
Anencephaly	13 (13.0%)	13 (13.0%)
Dandy-Walker malformation	10 (10.0%)	10 (10.0%)
Occipital encephalocele	8 (8.0%)	7 (7.0%)
Agenesis of the Corpus Callosum	7 (7.0%)	7 (7.0%)
Microcephaly	6 (6.0%)	6 (6.0%)
Hydrocephalus	6 (6.0%)	6 (6.0%)
Choroid plexus cyst	5 (5.0%)	5 (5.0%)
Spina bifida (meningocele)	5 (5.0%)	3 (3.0%)
Congenital Scoliosis	4 (4.0%)	4 (4.0%)
Chiari malformation	4 (4.0%)	4 (4.0%)
Schizencephaly	3 (3.0%)	3 (3.0%)
Hydranencephaly	3 (3.0%)	2 (2.0%)

Table 1: Diagnosis among the studied cases

There was significant moderate agreement between 2D and 3D regarding neurological anomaly diagnosis (**Table 2)**.

2D	3D		Total	
	Positive	Negative		
Positive	83 (83.0%) TP	0 (0.0%) FP	**83 (83.0%)**	
Negative	5 (5.0%) FN	12 (12.0%) TN	**17 (17.0%)**	
Total	**88 (88.0%)**	**12 (12.0%)**	**100 (100.0%)**	
Kappa		**0.799**	**P**	**<0.001***

Table 2: Agreement between 2D and 3D regarding neurological anomaly diagnosis

There was significant high agreement between 2D and 3D regarding Holoprosencephaly diagnosis **(Table 3).**

2D	3D		Total	
	Positive	Negative		
Positive	13 (13.0%) TP	0 (0.0%) FP	13 (13.0%)	
Negative	1 (1.0%) FN	86 (86.0%) TN	87 (87.0%)	
Total	14 (14.0%)	86 (86.0%)	100 (100.0%)	
Kappa	0.957		P	<0.001*

Table 3: Agreement between 2D and 3D regarding Holoprosencephaly diagnosis

There was significant perfect agreement between 2D and 3D regarding Anencephaly diagnosis (**Table 4)**.

2D	3D		Total	
	Positive	Negative		
Positive	13 (13.0%) TP	0 (0.0%) FP	13 (13.0%)	
Negative	0 (0.0%) FN	87 (87.0%) TN	87 (87.0%)	
Total	13 (13.0%)	87 (87.0%)	100 (100.0%)	
Kappa	1.000		P	<0.001*

Table 4: Agreement between 2D and 3D regarding Anencephaly diagnosis

There was significant perfect agreement between 2D and 3D regarding Dandy-Walker malformation diagnosis **(Table 5)**

2D	3D		Total	
	Positive	Negative		
Positive	10 (10.0%) TP	0 (0.0%) FP	10 (10.0%)	
Negative	0 (0.0%) FN	90 (90.0%) TN	90 (90.0%)	
Total	10 (0.0%)	90 (90.0%)	100 (100.0%)	
Kappa	1.000		P	<0.001*

Table 5: Agreement between 2D and 3D regarding Dandy-Walker malformation diagnosis

There was significant high agreement between 2D and 3D regarding Occipital encephalocele diagnosis **(Table 6)**.

2D	3D		Total	
	Positive	Negative		
Positive	7 (7.0%) TP	0 (0.0%) FP	7 (7.0%)	
Negative	1 (1.0%) FN	92 (92.0%) TN	93 (93.0%)	
Total	8 (8.0%)	92 (92.0%)	100 (100.0%)	
Kappa	0.928		P	<0.001*

Table 6: Agreement between 2D and 3D regarding Occipital encephalocele diagnosis

There was significant perfect agreement between 2D and 3D rsegarding Agenesis of the Corpus Callosum diagnosis (**Table 7)**.

2D	3D		Total	
	Positive	Negative		
Positive	7 (7.0%) TP	0 (0.0%) FP	7 (7.0%)	
Negative	0 (0.0%) FN	93 (93.0%) TN	93 (93.0%)	
Total	7 (7.0%)	93 (93.0%)	100 (100.0%)	
Kappa	1.000		P	<0.001*

Table 7: Agreement between 2D and 3D regarding Agenesis of the Corpus Callosum diagnosis

There was significant perfect agreement between 2D and 3D regarding Microcephaly diagnosis **(Table 8)**.

2D	3D		Total	
	Positive	Negative		
Positive	6 (6.0%) TP	0 (0.0%) FP	6 (6.0%)	
Negative	0 (0.0%) FN	94 (94.0%) TN	94 (93.0%)	
Total	6 (6.0%)	94 (94.0%)	100 (100.0%)	
Kappa	1.000		P	<0.001*

Table 8: Agreement between 2D and 3D regarding Microcephaly diagnosis

There was significant perfect agreement between 2D and 3D regarding Hydrocephalus diagnosis **(Table 9)**.

2D	3D		Total	
	Positive	Negative		
Positive	6 (6.0%) TP	0 (0.0%) FP	6 (6.0%)	
Negative	0 (0.0%) FN	94 (94.0%) TN	94 (93.0%)	
Total	6 (6.0%)	94 (94.0%)	100 (100.0%)	
Kappa	1.000		P	<0.001*

Table 9: Agreement between 2D and 3D regarding Hydrocephalus diagnosis

There was significant perfect agreement between 2D and 3D regarding Choroid plexus cyst diagnosis **(Table 10)**.

2D	3D		Total	
	Positive	Negative		
Positive	5 (5.0%) TP	0 (0.0%) FP	5 (5.0%)	
Negative	0 (0.0%) FN	95 (95.0%) TN	95 (95.0%)	
Total	5 (5.0%)	95 (95.0%)	100 (100.0%)	
Kappa	1.000		P	<0.001*

Table 10: Agreement between 2D and 3D regarding Choroid plexus cyst diagnosis

There was significant moderate agreement between 2D and 3D regarding Spina bifida (meningocele) diagnosis **(Table 11)**.

2D	3D		Total	
	Positive	Negative		
Positive	3 (3.0%) TP	0 (0.0%) FP	3 (3.0%)	
Negative	2 (2.0%) FN	95 (95.0%) TN	97 (97.0%)	
Total	5 (5.0%)	95 (95.0%)	100 (100.0%)	
Kappa	0.749		P	<0.001*

Table 11: Agreement between 2D and 3D regarding Spina bifida (meningocele) diagnosis

There was significant perfect agreement between 2D and 3D regarding Congenital Scoliosis diagnosis **(Table 12)**.

2D	3D		Total	
	Positive	Negative		
Positive	4 (4.0%) TP	0 (0.0%) FP	4 (4.0%)	
Negative	0 (0.0%) FN	96 (96.0%) TN	96 (96.0%)	
Total	4 (5.0%)	96 (96.0%)	100 (100.0%)	
Kappa	1.000		P	<0.001*

Table 12: Agreement between 2D and 3D regarding Congenital Scoliosis diagnosis

There was significant perfect agreement between 2D and 3D regarding Chiari malformation diagnosis **(Table 13)**.

2D	3D		Total	
	Positive	Negative		
Positive	4 (4.0%) TP	0 (0.0%) FP	**4 (4.0%)**	
Negative	0 (0.0%) FN	96 (96.0%) TN	**96 (96.0%)**	
Total	**4 (5.0%)**	**96 (96.0%)**	**100 (100.0%)**	
Kappa	**1.000**		**P**	**<0.001***

Table 13: Agreement between 2D and 3D regarding Chiari malformation diagnosis

There was significant perfect agreement between 2D and 3D regarding diagnosis **(Table 14)**.

2D	3D		Total	
	Positive	Negative		
Positive	3 (3.0%) TP	0 (0.0%) FP	**3 (3.0%)**	
Negative	0 (0.0%) FN	97 (97.0%) TN	**97 (97.0%)**	
Total	**3 (3.0%)**	**97 (97.0%)**	**100 (100.0%)**	
Kappa	**1.000**		**P**	**<0.001***

Table 14: Agreement between 2D and 3D regarding diagnosis

There was significant moderate agreement between 2D and 3D regarding Hydranencephaly diagnosis **(Table 15)**.

Diagnosis	Equivalent	More
Overall	61 (61.0%)	39 (39.0%)
Holoprosencephaly	9 (64.3%)	5 (35.7%)
Anencephaly	10 (76.9%)	3 (23.1%)
Dandy-Walker malformation	4 (40.0%)	6 (60.0%)
Occipital encephalocele	4 (50.0%)	4 (50.0%)
Agenesis of the Corpus Callosum	2 (28.6%)	5 (71.4%)
Microcephaly	6 (100.0%)	0 (0.0%)
Hydrocephalus	4 (66.7%)	2 (33.3%)
Choroid plexus cyst	1 (20.0%)	4 (80.0%)
Spina bifida (meningocele)	1 (20.0%)	4 (80.0%)
Congenital Scoliosis	3 (75.0%)	1 (25.0%)
Chiari malformation	2 (50.0%)	2 (50.0%)
Schizencephaly	2 (66.7%)	1 (33.3%)
Hydranencephaly	1 (33.3%)	2 (66.7%)

Table 15: Informative value of 3D over 2D in different diagnoses among the studied cases.

DISCUSSION

Central nervous system malformations are the second most frequent class of congenital anomaly, following congenital diseases of the heart. [12]

About 21% of congenital malformations of the CNS, including one of the most common congenital disorders and may occur either isolated or associated with other anomalies of the neural system itself or other systems. [3]

Central nervous system malformation are usually severe and considered the most common indications for therapeutic abortions. [4]

In modern obstetrics, screening for fetal anomalies has become one of the most profile health care issues. [6]

Diagnosis prenatally uses various invasive and noninvasive techniques to assess the health condition of the fetus or any disorder in intrauterine fetus. Ultrasonographic examination is an effective technique for antenatal diagnosis of these congenital anomalies. Patients usually accept this technique because it is not invasive method. An accuracy of ultrasonographic detection of CNS malformation is 92% to 99.7% according to several studies. [12]

In diagnosis of congenital anomalies, traditional two dimensional ultrasounds (2DUS) images may be confusing & difficult to construct to some clinicians because they must be interpreted to form a 3D impression of the anatomic structures available [14].

Three dimensional ultrasound (3DUS) has consider the new standard technique in antenatal diagnosis of fetal congenital anomalies. This technique allows examination of the fetal anatomy in more details and higher quality illusteration of congenital anomalies. [8]

Extensive and severe life threating disorders give reason for early termination of pregnancy, and detection of minor disorders helps everybody to be prepared and reassured for post-delivery management. [4]

The main purpose of our study is to assess the role of three dimensional (3D) ultrasound compared with two dimensional (2D) ultrasound in diagnosis of fetal central nervous system congenital malformations.

This prospective study which was performed at Obstetrics and Gynecology Department, Al-azhar University Hospital included 100 patients with gestational age from 18 weeks to 24 weeks by 2D ultrasound then examined by 3D ultrasound.

Each case was underwent serial transabdominal ultrasound examinations of fetal anatomy in details for detection of malformations of the neural, cardiovascular, gastrointestinal, muscloskeletal and genitourinary systems. Ultrasound examinations included transabdominal two-dimensional ultrasound examination was done first, then three-dimensional U/S examination.

Many factors, including the experience of the investigators, can directly influence this process. In some cases of complicated fetal malformations, it can be difficult, even for experienced sonologists, to accurately determine anatomic relationships. 3D US may help to solve these problems. [13]

3D US acquires a sequence of 2D images at relatively equal angles and distances; these images are precisely placed in the 3D volume data set. [13]

The current study revealed that out of 100 cases, 2D US made definite diagnoses of 83 malformations (83%). all of which were consistent with the postnatal or postmortem findings. 3D US established definite diagnoses of 88 malformations (88%).

The current study agrees with the study by Fatma et al., (2019) which reported that 3D ultrasonography is

effective in assessment of fetal CNS anomalies with detection of CNS anomalies on ultrasound was 90 %.

Our study found that the most common neurological malformations detected were Holoprosencephaly and Anencephaly which had significant high agreement between 2D and 3D regarding their diagnosis *(p value< 0.001)*.

These findings are in agreement with previous studies of Fatma et al., (2019) which revealed that Holoprosencephaly was the most prevalent malformation (13.33 %), followed by anencephaly (10 %) Dandy-Walker malformation (10 %) and hydrocephalus (6.66 %).

The current study revealed that there was significant agreement between 2D and 3D regarding the congenital fetal spinal and cranial malformations with p value < *0.001*.

The 2D and 3D ultrasound provided equal diagnostic information in microcephaly while 3D US provided more diagnostic information than 2D US for Choroid plexus cyst, corpus callosum agenesis and spina bifida (meningocele).

These results were in concordant with the study of Liu et al., (2005) which revealed that there is improved capability of 3D US to view the corpus callosum and the intracranial midline structures when compared with 2D US and 3D US visualized these structures in 78.1% of examinations; while 2D US visualized them in 3.1% of examinations. [18]

Our study revealed that the 3D US take the upper hand than 2D US in identifying small neurological malformations as choroid plexus cyst and Spina bifida.

These results were in agreement with the study done by Xu et al., (2002) which revealed that 3D US was superior to 2D US particularly in identifying the spine/extremities, cranium/face, malformations, and body surface explained by malformations of the cranium and spine are often associated with specific curved deformities that cannot be displayed completely on 1 cross sectional image. It is therefore difficult for conventional 2D US to display these malformations in the 3D shape and their relationships to neighboring structures. Hence, misdiagnosis and uncertain diagnosis may easily occur. [19]

On the contrary, Wang et al., (2000) found that 3DUS did not offer marked extra data over what was offered by 2DUS.

These results were concordant with the results of Mohamed et al., (2000) which reported that diagnosis of a case with small spina bifida was missed on routine 2-D ultrasound examination of the low risk women and diagnosis of spina bifida after 26 weeks gestation was suspected and confirmed by 3D imaging.

The increasing incidence of detection of CNS congenital anomalies in recent study may be explained by increased awareness amongst treating physicians and the progress and development of three dimensional (3D) ultrasound technology over the last years . [6]

Our results agreed with Dyson et al., (2000) who reported that, 3DUS introduced advantages over 2D US imaging in terms of diagnosis of some anomalies and data storage. However, it must be emphasized that, performing 2DUS before 3D US scanning is essential to localize the proper site for 3D scanning; consequently 3D US performance is impossible to be carried out without the prior use of 2D ultrasound. [2]

Thus, three-dimensional ultrasonography is not considered the only technique in screening but an adjunct to 2D ultrasonography for fetuses in which malformations are suspected or already determined during routine basic anomaly scan.

The main strength point of this current study is that it was done on large sample size in relation to the previous studies like Xu et al. (2002) which involved 41 fetuses and Fatma et al. (2019) which involved 30 cases. That helps in increase in diagnosis accuracy.

The limitations of the study are worthy of mention, The present 3D US technique still has some limitations, such as being affected by fetal motion, the amniotic fluid amount, and the orientation view.

CONCLUSION

In comparison with 2D US, 3D US improves the ability of diagnosis by introducing more information in diagnosis during fetal malformations evaluation, especially in illusteration of fetal small cranial anomalies and spina bifida. 3D US is a valuable adjunct to 2D US in prenatal diagnosis.

Three-dimensional ultrasonography is not considered the only technique in screening but an adjunct to 2D ultrasonography for fetuses in which malformations are suspected or already determined during routine basic anomaly scan.

Two dimensional ultrsonography remains the gold standard in assessment of fetal anomalies, and the three dimensional ultrasonography is not considered a screening technique alone but an adjunct to two dimensional ultrasonography for fetuses in whom disorders are suspected or already determined during routine anomaly scan of the fetus .

We recommend the adjunctive use of 3-D ultrasonography with the 2-D mode in selective cases to increase diagnostic accuracy of congenital mal - formation.

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