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Original article

Three dimensional/four-dimensional ultrasonography in detection of CNS and non-CNS anomalies in pregnant females with polyhydramnios

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Abstract

Background: A great concerns have been obtained for CNS anomalies due to their maternal and fetal morbidities and mortalities outcomes. The high prevalence of CNS anomalies has been linked to polyhydramnios in several studies. This study was conducted to evaluate the role of 3D/4D US in detection of CNS anomalies as compared to other non-CNS anomalies in pregnancy complicated with polyhydramnios. **Methods:** This was a cohort study conducted at the radiology department of University Hospital. The study was done on 110 pregnant females diagnosed with polyhydramnios. Regular visits and follow-up of patients were scheduled till either delivery or termination of pregnancy. **Results:** The most common fetal anomalies were CNS anomalies detected in 20 patients (18.18%) followed by

musculoskeletal anomalies in 6 patients (5.5%) then cardiovascular anomalies in 5 patients (4.5%). Chiari malformation represented the most common malformation affecting about 6 fetuses (5.5%) of all the participants. There was a significant agreement between antenatal diagnosis of congenital anomalies as detected by 3D/4D US and postnatal confirmation of the diagnosis. **Conclusions:** The gold standard technique in detection of fetal anomalies is 3D/4D ultrasonography with high accuracy especially in detection of CNS malformations. Also, the incidence of CNS malformation in pregnant females complicated with polyhydramnios is more than other non-CNS anomalies.

1. Introduction:

Children's future health may be affected by the quality of the amniotic fluid present during pregnancy and delivery. Polyhydramnios is characterized by an excessive amount of amniotic fluid relative to the gestational age of the fetus, and it has been linked to a number of fetal and maternal conditions. There is an increased risk of perinatal and maternal morbidity and mortality, including fetal death in utero, early labor, premature rupture of membranes, cord prolapse, fetal macrosomia, breech presentation, cesarean section, and postpartum hemorrhage [(1)]. Polyhydramnios is linked to multiple pregnancies, maternal diabetes mellitus, rhesus iso-immunization, congenital and chromosomal abnormalities, and other complications affecting the mother, the fetus, and the placenta. Idiopathic polyhydramnios is the label given when no prenatal etiology is identified, which occurs in as many as 70% of patients [(2)].

There is evidence linking polyhydramnios to a variety of different fetal abnormalities, including those affecting the central nervous system (CNS), the gastrointestinal tract (GI), and swallowing [(3)]. The rendering mode of 3D ultrasonography is beneficial for stereographic recognitions, notably of fetal

appearance, and it has seen widespread application in obstetrical therapeutic settings. Four-dimensional (4D) ultrasonography is the result of decades of improvements in both the resolution of 2D pictures and the capacity of image data processing, which have allowed for the creation of 3D images that are almost real-time [(4)] .

The aim of this work was to evaluate the role of 3D/4D US in detection of CNS anomalies as compared to other non-CNS anomalies in pregnancy complicated with polyhydramnios.

2. Methods:

This was a cohort study conducted at the radiology department of University Hospitals. The study was done within two years starting from April 2016 on 110 pregnant females diagnosed with polyhydramnios using 3D/4D probe (Toshiba, XARIO, 200, Japan) ultrasound after 16 weeks of gestation and followed up till labor to assess the pre-natal with the post-natal outcomes. Patients were subdivided into pregnant women with polyhydramnios and fetal anomalies (no=40) and pregnant women without fetal anomalies (no=70). We evaluated the incidence of CNS anomalies compared to other anomalies with regular visits and follow-up of patients scheduled till either delivery or termination of pregnancy. The post-natal findings were assessed based on clinical findings and different radiological modalities.

Calculation of amniotic fluid index (AFI) was assessed using 3D/4D US and those with AFI more than 25 were included in the study. We excluded from our study pregnant females diagnosed with intrauterine fetal death, gestational or pregestational DM and multifetal pregnancies.

Statistical analysis:

Descriptive data were reported as mean ± SD. Categorical variables were reported as counts and proportions. Univariate analysis included Fisher exact or Chi-square tests to compare categorical variables and T-test for scale data. All comparisons were two tailed, and $p < 0.05$ was considered statistically significant. Analyses were carried out using IBM SPSS version 25 statistical package.

Ethical considerations:

All data was anonymous and confidential. No one was obliged to participate in this study and all patients have the right to withdraw from the study at any time. All

permissions were taken from the included departments in the study.

3. Results:

Baseline Characters of the studies participants (table 1):

The mean age of cases with polyhydramnios and fetal anomalies was 32.5±4.344 with a minimum single pregnancy and maximum 4 previous pregnancies. They had a mean AFI 28.2±2.02801 and the minimum time of examination was within 16 week of gestation. Cases with polyhydramnios without fetal anomalies had an average age of 33.03±4.44 with a minimum single pregnancy and maximum 5 previous pregnancies. They had a mean AFI 27.9571±1.3772 and the minimum time of examination was 24 weeks of gestation. There was no statistically significant difference between both groups as regards to their baseline characteristics (P-value > 0.05).

Table (1): Age, number of pregnancies, offspring, and amniotic fluid index comparison between pregnant women with Polyhydramnios and fetal anomalies and pregnant women with Polyhydramnios without fetal anomalies:

Items		Mean±SD	P-value
Age	Polyhydramnios with fetal anomalies (no=40)	32.5±4.3	0.514
	Polyhydramnios without fetal anomalies (no=70)	33±4.4	
Number of pregnancies	Polyhydramnios with fetal anomalies (no=40)	2.6±0.9	0.148
	Polyhydramnios without fetal anomalies (no=70)	2.8±0.9	
Amniotic fluid index	Polyhydramnios with fetal anomalies (no=40)	28.2±2	0.457
	Polyhydramnios without fetal anomalies (no=70)	27.9±1.4	

Incidence of anomalies (Tables 2, 3) (figure1,2 and 3):

The most common was CNS anomalies detected in 20 patients (18.18%) followed by musculoskeletal anomalies in 6 patients (5.5%) then cardiovascular anomalies in 5 patients (4.5%). Only 5 fetuses (4.5%) had multiple anomalies of them 3 fetuses had CNS and associated anomalies and 2 fetuses had multiple non-CNS anomalies. There was a highly significant difference between the detection of CNS anomalies and other fetal anomalies.

Chiari malformation represented the most common malformation affecting about 6 fetuses (5.5%) of all the participants. Holoprosencephaly represented the 2nd most common malformation affecting 4 fetuses (3.6%) from all the participants. Dandy Walker malformation, esophageal atresia and achondroplasia represented the 3rd most common malformation affecting 3 fetuses (2.7%) of all the participants.

Table (2): Comparison between CNS anomalies and all other systems anomalies regarding their proportion.

Anomalies	Frequency (110)	Percent (100%)	P value
CNS anomalies	20	18.18	
CNS and associated anomalies	3	2.7	0.0002*
GIT anomalies	4	3.6	0.0005*
Musculoskeletal	6	5.5	0.002*
Cardiovascular	5	4.5	0.001*
Multiple non-CNS anomalies	2	1.8	0.0001*

P-value is significant

Table (3): Proportion of CNS and non-CNS anomalies among all participants.

Anomalies	Frequency (110)	Percent (100%)
CNS and associated anomalies Cyclopes and holoprosencephaly Unilateral multicyclic kidney, left atrium dilatation, hydrocephalus and Dandy Walker variant	3 1 1	2.7 0.9 0.9
Amniotic band syndrome and acrania	1	0.9
CNS anomalies	20	18.18
Chiari malformation	6	5.5
Hydrocephalus	2	1.8
Holoprosencephaly	4	3.6
Acrania	2	1.8
Dandy Walker	3	2.7
Corpus callosum agenesis and colpocephaly	1	0.9
Hydrocephalus and peri-ventricular leukomalacia	1	0.9
Hydrocephalus and lissencephaly	1	0.9
GIT anomalies	4	3.6
Esophageal atresia	3	2.7
Duodenal atresia	1	0.9
Musculoskeletal	6	5.5
Diaphragmatic hernia	1	0.9
Sacral agenesis and talipes	1	0.9
Achondroplasia	3	2.7
Cleft palate	1	0.9
Multiple non-CNS anomalies	2	1.8
Esophageal atresia Hypoplastic left ventricle, and ascites	1	0.9
Hydrops and Cystic hygroma	1	0.9
Cardiovascular	5	4.5
Cystic hygroma	1	0.9
Aortic coarctation	1	0.9
Cardiomegaly	1	0.9
Dextrocardia	1	0.9
Right ventricular dilatation and Cardiomegaly	1	0.9

The accuracy of 3D/4D in detection of anomalies (Table 4):

There was a significant agreement between antenatal diagnosis of congenital anomalies as detected by 3D/4D US and postnatal confirmation of the diagnosis. False positive results was detected only in 1 case diagnosed by the US as having Hydrocephalus and periventricular leukomalacia. False negative results were detected only in 1 case being free by antenatal US and confirmed to have cardiomegaly postnatally.

Table (4): Prenatal 3D/4D US diagnosis of congenital abnormalities compared to postnatal confirmation.

Anomalies	Antenatal 4D US (40)	Postnatal diagnosis	P value
CNS anomalies			
Chiari malformation	6 (15%)	6 (15%)	
Hydrocephalus	2 (5%)	2 (5%)	
Holoprosencephaly	4 (10%)	4 (10%)	
Acrania	2 (5%)	2 (5%)	
Dandy walker	3 (7.5%)	3 (7.5%)	
Corpus callosum agenesis and colpocephaly	1 (2.5%)	1 (2.5%)	
Hydrocephalus and periventricular leukomalacia	1 (2.5%)	0 (0%)	
Hydrocephalus and lissencephaly	1 (2.5%)	1 (2.5%)	
CNS and associated anomalies			
Cyclopes and holoprosencephaly	1 (2.5%)	1 (2.5%)	
Unilateral multicyclic kidney, left atrium dilatation, hydrocephalus and dandy walker variant	1 (2.5%)	1 (2.5%)	**0.002***
Amniotic band syndrome and acrania	1 (2.5%)	1 (2.5%)	
GIT anomalies			
Esophageal atresia	3 (7.5%)	3 (7.5%)	
Duodenal atresia	1 (2.5%)	1 (2.5%)	

Musculoskeletal			
Diaphragmatic hernia	1 (2.5%)	1 (2.5%)	
Sacral agenesis and talipes	1 (2.5%)	1 (2.5%)	
Achondroplasia	3 (7.5%)	3 (7.5%)	
Cleft palate	1 (2.5%)	1 (2.5%)	
Cardiovascular			
Cystic hygroma	1 (2.5%)	1 (2.5%)	
Aortic coarctation	1 (2.5%)	1 (2.5%)	
Cardiomegaly	1 (2.5%)	2 (5%)	
Dextrocardia	1 (2.5%)	1 (2.5%)	
Cardiomegaly and right ventricular dilatation	1 (2.5%)	1 (2.5%)	
Multiple non-CNS anomalies			
Hypoplastic left ventricle, ascites and esophageal atresia	1 (2.5%)	1 (2.5%)	
Cystic hygroma and hydrops	1 (2.5%)	1 (2.5%)	
Total	40 (100%)	40 (100%)	

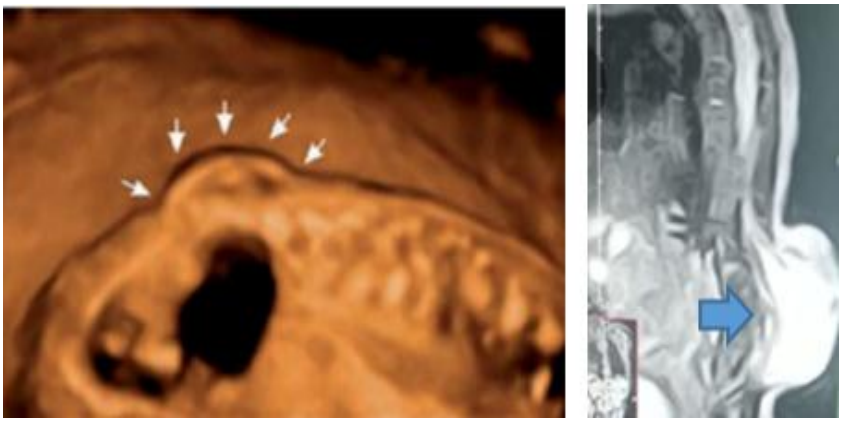

Figure 1: 3D image for the lumbar spine at sagittal plan (Left) shows lower back swelling (arrows) of meningocele and spina bifida (associating Chiari II malformation) and postnatal sagittal T2 WI (Right) for the lumbar spine confirming the US diagnosis.

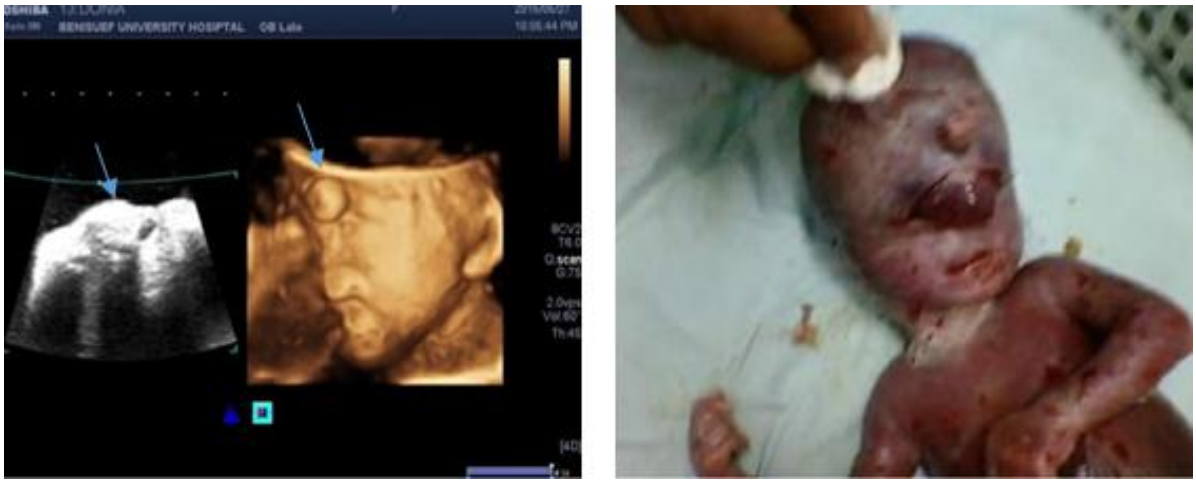

Figure 2: 2D and 3D images (left) showing cyclopia (arrows) and postnatal image (Right) confirming the US diagnosis

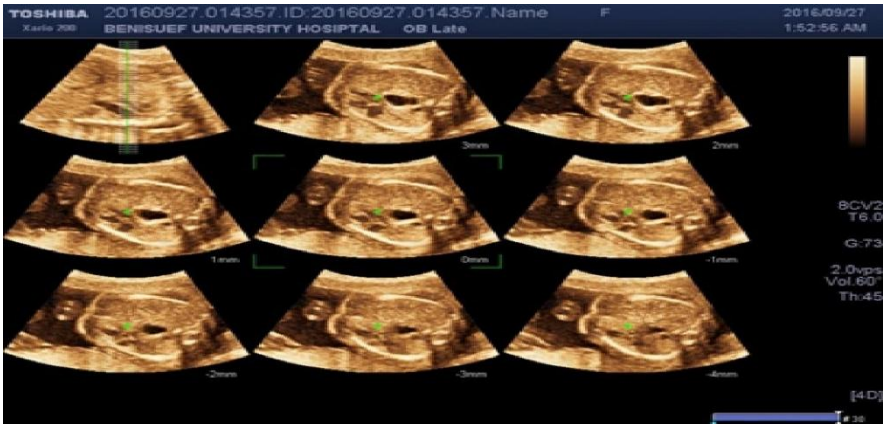

Figure 3: Section at level of the heart showing anechoic structure (stomach. Dotted) located posterior to the heart denoting diaphragmatic hernia)

4. Discussion:

Prenatal ultrasonography screening is now standard practice provided the necessary equipment and personnel are available. However, regular scanning is becoming more available in the first trimester, especially in high-resource settings, thus it is possible to undertake it as early as the first trimester. The major purpose of a fetal ultrasound anomaly scan using 4D ultrasonography in this day and age is to offer precise information that will assist the delivery of optimum prenatal care

with the best potential results for both the mother and the baby [5] .

Ultrasonography using 3D/4D techniques provides a gold standard for the antenatal diagnosis of congenital anomalies. This study demonstrated a significant agreement between antenatal diagnosis of congenital anomalies as detected by 3D/4D US and postnatal confirmation of the diagnosis. False positive results were detected only in 1 case diagnosed by US as having Hydrocephalus and periventricular leukomalacia. False negative result was detected only in 1 case being free by antenatal US and confirmed to have cardiomegaly postnatally.

Several studies have evaluated the role of 3D/4D ultrasonography in detection of fetal congenital anomalies during pregnancy like the study of Abozaid et al. who assessed the role of 3D/4D US in detection of brain anomalies and showed similar results to this study demonstrating that the disease detection rate was about (98%) with 100% sensitivity and specificity. In addition, Hassan et al. analyzed the performance of 4D US in detecting central nervous system malformation in fetuses, and they found that, using postnatal confirmation as a gold standard, ultrasonography can identify CNS fetal abnormality in 62 individuals (true positives). They determined that the overall sensitivity and diagnostic accuracy for identifying central nervous system fetal abnormality in the United States was 96.88% and 81%, respectively [7] .

Yu et al. investigated the prevalence of newborn malformations after induction of labor and natural delivery to assess the diagnostic usefulness of 2D and 3D US in detecting prenatal defects. Data for 4D-US showed accuracy, sensitivity, and specificity of 93.59, 90.80, and 93.70 compared to 81.40, 43.68, and 82.92 for 2D-US. They concluded that 4D-US achieved obviously higher accuracy, sensitivity, and specificity especially if combined with 2D US [8] . The study of Duc et al. evaluated the detection of fetal central nervous system anomalies using magnetic resonance imaging and ultrasound and found a significant agreement between 3D US and fetal MRI in detection of CNS anomalies [9] .

The benefits of US in detecting fetal malformations may be explained by its high resolution, low cost, and safety for both the mother and the baby throughout pregnancy. When compared to other imaging modalities, ultrasound shines in the context of pregnancy because to its versatility and the fact that it may be utilized as early as the first trimester to monitor fetal movement in

near real time. Ultrasound, and especially 3D/4D US, is among the greatest non-invasive diagnostic methods available for the diagnosis and observation of prenatal abnormalities and disorders. As 3D/4D technology has advanced, prenatal diagnosis of fetal abnormalities and syndromes has moved far earlier into the pregnancy, often occurring in the first trimester [(10)].

This study also compared between fetal CNS anomalies and other anomalies and found that the most common fetal anomalies was CNS anomalies detected in 20 patient (18.18%) followed by musculoskeletal anomalies in 6 patients (5.5%) then cardiovascular anomalies in 5 patients (4.5%). Only 5 fetuses (4.5%) had multiple anomalies of them 3 fetuses had CNS and associated anomalies and 2 fetuses had multiple non-CNS anomalies. There was a highly significant difference between the detection of CNS anomalies and other fetal anomalies.

The great interest with CNS malformation was due to the fact that due to their association with significant morbidity and mortality, as well as their potential to affect neurocognitive and motor development in survivors, such abnormalities are of clinical significance. Therefore, evaluating the fetal central nervous system throughout pregnancy is crucial. The growth of the fetus should be monitored throughout pregnancy, and the parents should be counseled on fetal treatments, delivery, and postnatal care and prognosis if necessary [(7)].

In this study, Chiari malformation represents the most common malformation affecting about 6 fetuses (5.5%) of all the participants. Holoprosencephaly represents the 2nd most common malformation affecting 4 fetuses (3.6%) from all the participants. Dandy Walker malformation, esophageal atresia and achondroplasia represent the 3rd most common malformation affecting 3 fetuses (2.7%) of all the participants.

In agreement with our results was the study of Adel et al. about the value of 3D/4D US in detection of neural anomalies who reported that of 120 pregnant females only 14 cases had Chiari malformation, 6 cases had holoprosencephaly, and 4 cases had Dandy Walker malformation. They also found that most cases were isolated anomalies; 7 cases (7%) had associated anomalies [(11)].

Also, Lalchan et al. in their study about the prevalence of congenital

anomalies in polyhydramnios revealed that among the various congenital malformations diagnosed by ultrasonography; central nervous system (CNS) including meningomyelocele, hydrocephalus, and holoprosencephaly, Gastrointestinal (GI) including esophageal and duodenal atresia and Skeletal malformations were the commonest [(12)].

Kornacki et al. observed that 13.8% of women with polyhydramnios had a congenital anomaly, with the most common being deformities of the central nervous system or digestive tract. Most often, three fetuses (3.2% of the total) were diagnosed with CDH; two of them were born to mothers with moderate polyhydramnios, while the other two were born to mothers with severe polyhydramnios [(13)].

Tashfeen & Hamdi, in their study evaluating polyhydramnios as a predictor for neonatal outcomes revealed that Hydrocephalus, anencephaly, holoprosencephaly, and myelomeningocele were among the CNS defects identified in 12 pregnancies. Ten pregnancies were identified with gastrointestinal abnormalities, such as esophageal and duodenal atresia, diaphragmatic hernia, and trachea esophageal fistula. Malformations of the heart, blood vessels, or lungs were present in eight pregnancies. These malformations ranged from structural heart defects to hydrops to pulmonary edema. Multiple organ systems, including the brain, digestive tract, and urinary tract, were affected in four prenatal cases [(14)].

In contrast to our results was the cross-sectional study conducted by Sundaram et al. about the benefits of US in decreasing the maternal and fetal morbidity and mortality. They found that heart problems accounted for 40.38 percent of all birth malformations, with neural tube defects coming in second at 25.0 percent, and gastrointestinal anomalies in third at 18.27 percent [(15)].

Also, the study of Alia & Ahmed, about the prevalence of congenital anomalies in Madina Saudi Arabia during the period from January to December 2009 evaluated a total of 2890 prenatal ultrasounds out of them 86 cases of congenital abnormalities were identified the majority were from central nervous system (54.65%), followed by Musculo-skeleton (38.6%) [(16)].

The high prevalence in their studies could be explained as the percentage was from cases only not from all the participants. Also, the difference in the inclusion criteria

as they included all pregnant females including normal pregnancies, polyhydramnios and diabetic females.

5. Conclusions:

The gold standard technique in detection of fetal anomalies is 3D/4D ultrasonography with high accuracy especially in detection of CNS malformation. Also, the incidence of CNS malformation in pregnant females complicated with polyhydramnios is more than other non-CNS anomalies.

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