Role of 4D Ultrasound in the Diagnosis of Intra-Uterine Cranio-Facial Anomalies

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Abstract

Background: Craniofacial anomalies account for approximately one-third of all birth defects and are a significant cause of infant mortality. They include brain, cranial bone & facial anomalies. Ultrasound examination is an effective modality for the prenatal diagnosis of these anomalies. 3D/4D US offers several image displays for precise demonstration of the normal and abnormal anatomy of the fetus. Subtle or inconclusive Ultrasound abnormalities can be confirmed or ruled out by MRI.

Aim of the Work: To evaluate role of the 4D ultrasound in diagnosis of in utero congenital cranio-facial anomalies.

Patients and Methods: The study was conducted on 20 pregnant females with suspected congenital head anomalies by 2D ultrasound in Tanta University Hospitals at the Radiodiagnosis department. The cases were collected during a period starting from December 2015 to January 2017. All patients were subjected to 2D and 4D ultrasound examination.

Results: As regards to brain anomalies, sensitivity of 4D ultrasound = 94.74%, specificity of 4D ultrasound = 100%, PPV = 100%, NPV = 50.0 % & accuracy = 95%. As regards to cranial bone anomalies, sensitivity of 4D ultrasound = 100%, specificity = 100 %, PPV = 100%, NPV = 100 % & accuracy = 100%. As regards to facial anomalies, sensitivity of 4D ultrasound = 100%, specificity = 100 %, PPV = 100%, NPV = 100 % & accuracy = 100%. So 4D ultrasound is more superior to 2D ultrasound in demonstrating anomalies of the face, cranial bone (mainly through surface rendering mode) and brain (through multiplanar & tomographic views) which may affect the post natal outcome.

Conclusion: 4D US is considered now an important diagnostic tool in fetal medicine as it provides many advanced diagnostic options like multiplanar, multiview or tomographic imaging, volume calculation and surface rendering mode which aided in early diagnosis of fetal anomalies and improved postnatal outcome.

Key Words: Fetal – 4D – 2D – Ultrasound – Anomalies – Face – Brain.

Introduction

CRANIOFACIAL anomalies account for approximately one-third of all birth defects and are a significant cause of infant mortality. They include brain, cranial bone and facial anomalies. Since the majority of the bones, cartilage and connective tissues that comprise the head and face are derived from a multipotent migratory progenitor cell population called the neural crest, craniofacial disorders are typically attributed to defects in neural crest cell development [1].

Facial clefts are by far the most frequent among these malformations with an estimated incidence of about 0.1% births [2]. Ultrasound examination is an effective modality for the prenatal diagnosis of the CNS & facial anomalies. An accurate fetal diagnosis depends upon a precise description of the brain & face sonographic appearance and careful evaluation for associated malformations, which are often present [3].

In contrast to conventional 2-dimensional (2D) US that only allows imaging of single plane, 3D/4D US offers several image displays (e.g. the multiplanar view, tomographic view, surface view, transparent view & Volume Contrast Imaging) that do not exist in 2D imaging offering a precise demonstration of the normal and abnormal anatomy of the fetus. Digital storage of volumes permits virtual examinations by reloading of volumes and navigating through them in the absence of the patient [4].

Patients and Methods

The study was conducted on 20 pregnant females with suspected congenital head anomalies by 2D ultrasound in Tanta University Hospitals at the Radiodiagnosis Department. The cases were collected during a period starting from December 2015 to January 2017. The maternal age ranged
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from 18 to 33 years with mean age about 25.75 years.

I- Ultrasound examination:
2D ultrasound examination:
All patients were initially scanned by two-dimensional trans-abdominal probe using a TOSHIBA Aplio 500 ultrasound equipment with a convex abdominal transducer (3-5MHz.), the 2D US scans were used to identify & localize the region of interest (site of suspected anomalies) whether in the brain, face or other body systems.

4D ultrasound examination:
Once a craniofacial anomaly is suspected in the 2D examination, 4D examination was done using 4D trans-abdominal transducer to obtain an ultrasound volume. Trans-vaginal 4D probe was used in cases of deeply engaged head, fetus with unfavourable position for transabdominal 4D examination, occipitoanterior position with head not facing the transabdominal probe, and the face is inaccessible abdominally to be well examined.

4D protocol:
Taking an image for each patient in 4D mode was done in the following steps: (1) Starting examination by pressing 4D button in the keyboard. (2) Setting and adjusting the ROI. For taking good images, the head must be surrounded by an adequate amount of amniotic fluid the 4D volume box was adjusted to include the whole region of interest (head), (3) Adjusting the flexible cut line & placing the cut line of the volume box in the amniotic fluid, (4) Pressing 4D button or 4D live in the other menu on the touch panel, the volume was acquired, in the axial view.

Volumes were acquired during fetal quiescence. Acquisition time ranged from 2 to 6s per volume, and acquisitions were repeated if fetal movement occurred during acquisition.

Then the multiplanar mode was used to examine the brain and face in the three orthogonal planes (axial, sagittal and coronal planes) in some cases, it was necessary to modify the brightness and contrast settings of the multiplanar images to correct their resolution.

Multiview mode was also used as multiple planes (up to 16) of a volume were displayed simultaneously in multiview mode, similar to CT or MRI, with multilevel cuts every 1mm or less confirming the absence of falx cerebri in all levels to exclude holoprosencephaly and differentiate its types, also the multiview option helped in demonstration of posterior fossa anomalies by tracing its structures in different cuts and detection of any abnormal communication between 4th ventricle and cisterna magna, also it helps in the tracing of midline structures as corpus callosum and evaluation of cranial bone and facial abnormalities.

4D surface rendering mode was used to examine the facial structures (eyes, nose, lips & ears) and limbs. 4D maximum mode was used to evaluate skeletal structure of the bony face and clavicular bone. Abnormality in the brain visualized by 2D like absence of skull bone (anecephaly), cystic structure in occipital region (encephalocele) best visualized by 4D surface rendering.

Adjusting the image, using different 4D options: Rotating, zooming, panning and cutting out the undesired portion of the 4D image.

4D examination time was from 30 minute to 45 minute. Finally observation of the stored images for previous examination in 4D mode by pressing patient browser button, selecting main menu, selecting 4D data then selecting view option from the touch screen offline analysis of the images done for better analysis of the abnormalities seen in initial examination. The entire brain and face anatomy was analyzed. Only images with an acceptable quality of the brain and face were included in the study.

II- Interpretation and outcome measures:
All cases were followed up postnatally and the abnormality diagnosed by an obstetrician. Postnatal data was considered as the golden standard for accuracy of 2D & 4D findings.

Statistical analysis of the data [5]:
Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) [6] Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level.

Results

According to the maternal age: The maternal age ranged from 18 to 33 years with 12 cases above or equal the age of 25 years (60% ≥25 years old), and 8 cases below age of 25 years (40% <25 years old).

According to fetal gender: 11 fetuses (55%) were males and 9 fetuses (45%) were females. According to the gestational
age ranged from 15 to 39 weeks with Mean ± SD. = 27.45±7.13 weeks & median age = 25 weeks.

Out of the 20 pregnant females, 11 cases (55%) were in the second trimester and 9 cases (45%) were in the third trimester.

Out of the 20 pregnant women, 9 cases (45%) were diabetic, 5 cases were hypertensive (25%) and 6 cases with no past medical history of systemic disease.

According to the maternal obstetric history: out of 20 pregnant females, 6 cases were primigravida (30%) and 14 cases were multigravida (70%).

Out of 20 anomalies, 2 anomalies (10%) were alobar holoprosencephaly; one of them associated with hypototelism & anal atresia and the other one was associated with cleft lip; 2 anomalies (10%) were Anencephaly, 2 anomalies (10%) were exencephaly, 2 anomalies (10%) were Aqueductal stenosis, 2 anomalies (10%) were chiari malformation with its two types I & II, 3 anomalies (15%) were Dandy walker continuum (1 case was dandy walker malformation associated with microagnathia and 2 cases were dandy walker variant, one of them was associated with cleft lip, microcephaly & duodenal atresia and the other was isolated dandy walker variant).

Three anomalies were hydranencephaly (one of them showed that the whole brain tissue replaced by fluid with atrophic posterior fossa indicating severe ischemic insult and was associated with club foot while the other case was associated with renal agenesis, duodenal atresia and hypotelorism) (15%), 1 cleft lip (5%), 1 Cephalocele (5%), 1 hemifacial microsomia with acrania (5%) (asymmetry between both eyes, cleft lip with abnormal cranial bone), 1 case was obstructive hydrocephalus distal to 4th ventricle (obstruction of foramen of luschka & magendi) (5%).

Out of 20 cases, 19 cases (95%) showed cranial anomalies with affection of brain and cranial bone while 8 cases (40%) showed abnormalities in face (cleft lip - microagnathia - hypotelorism) and 6 cases (30%) showed affection of other systems (duodenal atresia, clubfoot, anal atresia and renal agenesis).

There was statistically significant difference in the relation between medical history and amount of amniotic fluid MCp=0.005. Out of 6 cases with no past medical history of systemic diseases, 5 cases (83.3%) showed normal amniotic fluid and 1 case (16.7%) showed decreased amniotic fluid.

Out of 9 diabetic cases, 5 cases (55.6%) showed increased amniotic fluid and 4 cases (44.4%) showed normal amniotic fluid. All the 5 hypertensive cases (100%) showed increased amniotic fluid.

As regards to brain anomalies, postnatal data revealed that about 19 cases out of 20 were positive for brain anomalies.

As regards to brain anomalies, 2D ultrasound findings revealed that out of the 19 cases about 14 cases (26.3%) were true positive (definitely diagnosed by 2D) while 5 cases (73.7%) were false negative (2D revealed abnormality but didn't reach definitive diagnosis) → sensitivity of 2D ultrasound for brain anomalies = 73.68%, specificity of 2D ultrasound for brain anomalies = 100%, PPV = 100%, NPV = 16.67% & accuracy = 75%.

As regards to brain anomalies, 4D ultrasound findings revealed that out of the 19 cases, about 18 cases (94.7%) were true positive (definitely diagnosed by 4D) while 1 case (5.3%) was false negative (4D revealed abnormality but didn't reach definitive diagnosis) → sensitivity of 4D ultrasound for brain anomalies = 94.74%, specificity of 4D ultrasound for brain anomalies = 100%, PPV = 100%, NPV = 50.0% & accuracy = 95%.

As regards to cranial bone anomalies, postnatal data revealed that about 6 cases out of 20 were positive for cranial bone anomalies.

As regards to cranial bone anomalies, 2D ultrasound findings revealed that out of the 6 cases about 4 cases (66.7%) were true positive (definitely diagnosed by 2D) while 2 cases (33.3%) were false negative (2D revealed abnormality but didn't reach definitive diagnosis) → sensitivity of 2D ultrasound for cranial bone anomalies = 66.67%, specificity of 2D ultrasound for cranial bone anomalies = 100%, PPV = 100%, NPV = 87.5% & accuracy = 90%.

As regards to cranial bone anomalies, 4D ultrasound findings revealed that out of the 6 cases, about 6 cases (100%) were true positive (definitely diagnosed by 4D) → sensitivity of 4D ultrasound for cranial bone anomalies = 100%, specificity of 4D ultrasound for cranial bone anomalies = 100%, PPV = 100%, NPV = 100% & accuracy = 100%.

As regards to facial anomalies, postnatal data revealed that about 8 cases out of 20 were positive for facial anomalies.

As regards to facial anomalies, 2D ultrasound findings revealed that out of the 8 cases about 4 cases (50%) were true positive (definitely diagnosed by 2D) while 2 cases (50%) were false → sensitivity
of 2D ultrasound for facial anomalies = 50%,
specificity of 2D ultrasound for cranial bone
anomalies = 100%, PPV = 100%, NPV = 75% &
accuracy = 80%.

As regards to facial anomalies, 4D ultrasound
findings revealed that out of the 8 cases, about 8
cases (100%) were true positive (definitely diag-
nosed by 4D) → sensitivity of 4D ultrasound for
facial anomalies = 100%, specificity of 4D ultrasonic
for facial anomalies = 100%, PPV = 100%,
NPV = 100% & accuracy = 100%.

As regards to other systems anomalies, postnatal
data revealed that about 4 cases out of 20 were
positive for other systems anomalies.

As regards to other systems anomalies, 2D
ultrasound findings revealed that all cases (100%)
were true positive (definitely diagnosed by 2D)
while 2 cases (50%) → sensitivity of 2D ultrasound
for other systems anomalies = 100%, specificity
= 100%, PPV = 100%, NPV = 100% & accuracy
= 100%.

As regards to other systems anomalies, 4D
ultrasound findings revealed that out of the 4 cases,
1 case (25%) was true positive (definitely diagnosed
by 4D) which was a case of talipes equinovarus
while 3 cases (75%) were false negative (4D didn't
reach definitive diagnosis) → sensitivity of 4D
ultrasound for other systems anomalies = 25%,
specificity of 4D ultrasound for other systems =
100%, PPV = 100%, NPV = 84.21% & accuracy
= 85%.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25</td>
<td>8</td>
<td>40</td>
</tr>
<tr>
<td>≥25</td>
<td>12</td>
<td>60</td>
</tr>
<tr>
<td>Min. – Max.</td>
<td>18-33</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD.</td>
<td>25.75±4.96</td>
<td></td>
</tr>
</tbody>
</table>

Table (2): Distribution of the studied cases according to
diagnosis (n=20).

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalocele</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Holoprosencephaly</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Anencephaly</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Aqueductal stenosis</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Chiari</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Cleft lip</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Dandywalker (malformation &amp; variant)</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>Excencephaly</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Hemifacial microsomia</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Hydranencephaly</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>Obstructive hydrocephalus distal to 4th ventricle</td>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>

Table (3): Distribution of the studied cases according to the
affected body system (n=20).

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>No.</th>
<th>%</th>
<th>Yes</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cranial</td>
<td>1</td>
<td>5</td>
<td>19</td>
<td>95</td>
<td></td>
</tr>
<tr>
<td>Facial</td>
<td>12</td>
<td>60</td>
<td>8</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Other body systems</td>
<td>14</td>
<td>70</td>
<td>6</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>

Table (4): Relation between medical history and amount of
Aminiotic fluid.

<table>
<thead>
<tr>
<th>Medical history</th>
<th>AF</th>
<th>DM</th>
<th>HTN</th>
<th>χ²</th>
<th>MCP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Decreased</td>
<td>1</td>
<td>16.7</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Normal</td>
<td>5</td>
<td>83.3</td>
<td>4</td>
<td>44.4</td>
<td>0</td>
</tr>
<tr>
<td>Increased</td>
<td>0</td>
<td>0.0</td>
<td>5</td>
<td>55.6</td>
<td>5</td>
</tr>
</tbody>
</table>

χ² and *-values for Chi square test.
MCP: *-value for Monte Carlo for Chi square test.
*: Statistically significant at p ≤ 0.05.

Table (5): Agreement (sensitivity, specificity) for brain anom-
algies.

<table>
<thead>
<tr>
<th>Brain</th>
<th>Postnatal data</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>2D US:</td>
<td>Negative</td>
<td>100</td>
<td>5</td>
<td>26.3</td>
<td>73.7</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Positive</td>
<td>0</td>
<td>14</td>
<td>73.7</td>
<td>26.3</td>
<td>100</td>
</tr>
<tr>
<td>4D US:</td>
<td>Negative</td>
<td>100</td>
<td>1</td>
<td>5.3</td>
<td>94.7</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Positive</td>
<td>0</td>
<td>18</td>
<td>94.7</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Table (6): Agreement (sensitivity, specificity) for cranial bone
anomalies.

<table>
<thead>
<tr>
<th>Cranial bone</th>
<th>Postnatal data</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>2D US:</td>
<td>Negative</td>
<td>100</td>
<td>2</td>
<td>33.3</td>
<td>66.7</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Positive</td>
<td>0</td>
<td>4</td>
<td>66.7</td>
<td>33.3</td>
<td>100</td>
</tr>
<tr>
<td>4D US:</td>
<td>Negative</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Positive</td>
<td>0</td>
<td>6</td>
<td>100</td>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>
Table (7): Agreement (sensitivity, specificity) for face anomalies.

<table>
<thead>
<tr>
<th>Postnatal data</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative (n=12)</td>
<td>12 100 4 50</td>
<td>50 100 75 80</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive (n=8)</td>
<td>0 0 4 50</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2D US:

<table>
<thead>
<tr>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>100</td>
<td>4</td>
<td>50</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>4</td>
<td>50</td>
</tr>
</tbody>
</table>

4D US:

<table>
<thead>
<tr>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>100</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>8</td>
<td>100</td>
</tr>
</tbody>
</table>

Table (8): Agreement (sensitivity, specificity) for other systems anomalies.

<table>
<thead>
<tr>
<th>Postnatal data</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative (n=16)</td>
<td>16 100 0 0</td>
<td>100 100 100 100</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive (n=4)</td>
<td>0 0 4 100</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2D US:

<table>
<thead>
<tr>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>100</td>
<td>3</td>
<td>75</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>1</td>
<td>25</td>
</tr>
</tbody>
</table>

4D US:

<table>
<thead>
<tr>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>100</td>
<td>8</td>
<td>100</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>1</td>
<td>25</td>
</tr>
</tbody>
</table>

Case (1):

Pregnant female aged 19 years presented 26 weeks of gestation without any prior antenatal checkups.

US findings:

2D US coronal image of fetal face with prominent eye balls, absent cranium and rudimentary brain.

Diagnosis: Anencephaly.

Case (2):

A 33-years-old female, with no family history of congenital anomalies, was referred for routine ultrasound examination at 26 weeks.

US findings:

2D ultrasound image (oblique views) of the fetal face with unilateral cleft lip.

Tomographic 4D axial US images confirming absent cranium and rudimentary brain.

Fig. (2): Tomographic axial 4D US images.

Fig. (3): Surface rendering 4D US image of the fetal head.

Surface rendering 4D US images of the fetal head with prominent eye balls, absent cranium and rudimentary brain giving frog like appearance of the fetal face.
Surface rendering 4D US image of the fetal head shows left sided cleft lip.

Diagnosis: Left sided cleft lip.

Case (3):
A pregnant female aged 18 years presented 35 weeks of gestation past medical history and family history were un-remarkable, for a routine antenatal checkup without any previous ultrasonography examinations.

US findings:
2D ultrasound (axial view) of the brain demonstrated single monoventricle, absent falx and fused thalami.

Fig. (6): 2D ultrasound (axial view) of the brain.

Surface rendering 4D US image of the fetal brain shows single monoventricle and fused thalami.

Fig. (7): Surface rendering 4D US image of the fetal brain.

Surface rendering 4D US image of the fetal face shows buffy odematous face.

Fig. (8): Surface rendering 4D US image of the fetal face.

Case (4):
A pregnant woman aged 33 years presented 22 weeks of gestation Past medical history and family history were un-remarkable, for a routine antenatal checkup without any previous ultrasonography examinations.

US findings:
2D ultrasound (sagittal view) of the brain demonstrated a large cystic mass filling the entire cranial cavity, present falx and normal posterior fossa.

Fig. (9): 2D ultrasound (sagittal view) of the brain.

Tomographic 4D US images revealed a large cystic mass filling the entire cranial cavity, present falx and normal posterior fossa.

Surface rendering 4D US images of the fetal face revealed normal face.

Diagnosis: A case of hydranencephaly.
Discussion

The application of 3D/4D ultrasound has been proven to increase diagnostic accuracy when applied to the study of the central nervous system (neuron scan) and orofacial malformations [7,8]. The incidence of congenital anomalies is directly proportional to the maternal age. In this study, about 60% of cases above 25 years which was similar to study by Al-Najjar, 2016 [9] and DrRaviteja et al., 2015 [10]. On contrary, Chen et al., 2007 [11] found that teenage pregnancy was significantly associated with increased risk of central nervous system anomalies.

The incidence of congenital anomalies increases with multigravida more than primigravida. In this study, 14 cases out of 20 were multigravida (70.0%) which matched with the results of Al-Najjar, 2016 [9]. On the other hand, Laharwal et al., 2016 [12] found that the incidence of neural tube defects was increased in children of primigravida.

In the current study, out of 20 anomalies 11 fetuses (65%) were males which agreed to study by Sarkar et al., 2013 [13] and El-Hamid et al., 2015 [14].

In the current study, out of 20 anomalies about 5 anomalies (25%) were acrania/exencephaly/anencephaly so acrania was the commonest anomaly detected which was similar to study by Behairy and Talaat, 2012 [15]. Also Liu et al., 2005 [16] stated that 3D US may contribute to early detection of fetal acrania, Chaoui et al., 2011 found that 4D US helps in diagnosis and localization of encephalocele [17].

The current study revealed that there was a statistically significant difference between accuracy of 4D compared to 2D ultrasound in detection of brain, cranial bone and facial abnormalities and the 4D added information in the diagnosis of these abnormalities to 2D ultrasound, in concordance with El-Mowafi, 2016 who studied 72 anomalies and found that 16 cases (22%) that had not been identified adequately at 2D US were disclosed with real-time 4D US and real-time 4D US gave further information in 18 cases (25%) [18].

Kalache et al., 2006 stated that three-dimensional Multi-Slice View can deliver informative images of the region of interest regardless of fetal position. It is particularly helpful for evaluation of complex fetal anomalies [19].

Xu et al., 2002 and Dyson et al., 2000 [20,21] stated that 3DUS was able to discover some complicated fetal malformations that were missed by 2D US and to determine the fetal malformations more precisely than 2D US did. Dyson et al., 2000 reported that 3D US images provided additional information in about 51% of cases and was equivalent to 2D US images in about 45% of cases. Additional information provided by 3D/4D US images impacted clinical management in 5% of patients [21].

Xu et al., 2002 assessed the fetuses with abnormalities both by (2D) and (3D) sonography and
2D US made definite diagnoses of 49 out of 62 malformations (79%) while 3D US established definite diagnoses of 58 malformations (94%; \( p < 0.01 \)). In 35 (60%) of the 58 malformations revealed by both 3D US and 2D US, the former provided more diagnostic information than the latter, all of which were consistent with the postnatal or postmortem findings which agreed with the present study as there is a statistically significant difference between 2D & 4D findings (\( p < 0.001 \) for brain anomalies, \( p = 0.02 \) for cranial bone anomalies & \( p = 0.009 \) for facial anomalies) [20].

Yigiter et al., 2007 [22] found that 3D US images provided additional information and confirmed diagnoses in 130 (69%) anomalies, 2D US images equivalently confirmed the diagnosis in 60 (31%) anomalies and were not disadvantageous in any of the cases which matched with the current study. Merz et al., 1995 examined 204 patients with 3D US and proved that 3D US is advantageous in demonstrating fetal defects [23].

Merz, 2006 [24] found that the 3D ultrasound provided conclusive detection of fetal defects in 4.2% of cases (42 of 1012), whereas the 2D technique failed to provide this information. Merz and Welter, 2005 studied 906 anomalous fetuses and demonstrated that 3D/4D US was advantageous, in 60.8% of cases when compared with 2D US [25].

As regards to brain anomalies, Yigiter et al., 2007 found that 3D US images provided additional information in 43 of 61 cases (70.49%) of CNS anomalies including holoprosencephaly, hydrocephalus, encephalocele and neural tube defects which agreed with the current study [22].

Rizzo et al., 2011 multicenter study found the following values for the detection of fetuses with CNS defects: The sensitivity 93.3% with a specificity of 96.5% with an excellent intercenter agreement while in the present study sensitivity of 4D in detection of brain anomalies was 94.74% & specificity was 100% [26].

As regards to facial anomalies, Azumendi et al., 2007 [27] stated that the fetal face can be visualized and analyzed only to a limited extent using 2D sonography because of the curvature and small anatomical details while 3DUS provides spatial reconstruction of fetal face and simultaneous visualization of all facial structures such as the fetal nose, eyebrows, mouth, and eyelids which matched with the results of the current study.

Mueller et al., 1996 compared 2DUS and 3DUS for diagnosis of central nervous system anomalies in 11 fetuses with ventriculomegaly (n=4), encephaly (n=1) spina bifida (n=5), and encephalocele (n=1) an erroneous diagnosis of encephalocele by 2D US was corrected as a cervical meningomyelocele when the examination was performed by 3D US [28].

Wang et al., 2000 reported on the improved ability of 3D US to visualize the intracranial midline and corpus callosum when compared with 2D US [29].

On contrary, other investigators found that 3D/4D US imaging did not provide significant additional information compared with 2D US. Scharf et al., 2001 [30] and Benacerraf, 2006, revealed that 3D ultrasound was insufficient as a primary tool to study fetuses at high risk for anomalies [31].

**Conclusion:**

4D US is considered now an important diagnostic tool in fetal medicine as it provides many advanced diagnostic options like multiplanar, multiview or tomographic imaging, volume calculation and surface rendering mode which aided in early diagnosis of fetal anomalies and improved postnatal outcome. The value of 4D ultrasound is undisputable in certain cases, such as facial clefts, brain anomalies, and spinal defects so it is time to recommend it in routine obstetrical examination.

**References**


Role of 4D Ultrasound in the Diagnosis of Intra-Uterine Cranio-Facial Anomalies

دور السونار رباعي الأبعاد في تشخيص العيوب الخلقية برأس وجه الجنين

التشوهات برأس وجه الجنين هي مجموعة من تشكّيات في نحو الرأس وانظام الوجه تشمل تشوهات الجهاز العصبي وتشوهات الوجه والتي تشمل الأنواع الأكثر شيوعاً منها ما يلي: شفة و/أو الحنك المشقوق والذي يحدث في الشفة أو الحنك (سقف الفم) أو كليهما، وتشوهات الجهاز العصبي الرتيبة الثانية من التشوهات الخلقية الأكثر شيوعاً بعد أمراض القلب الخلقية. ويعتبر الفحص بالموجات فوق الصوتية طريقة فعالة لتشخيص هذه التشوهات الخلقية قبل الولادة. ويعتمد التشخيص الدقيق لهذه التشوهات على الوصف الدقيق لمظهر الجهاز العصبي المرتبطة بالموجات فوق الصوتية والمقاييس الدقيقة لتشوهات الدماغ والموجهات المرتبطة به والتي غالباً ما تكون موجودة. ويعتبر الفحص بالموجات فوق الصوتية هو الطرق المفضلة في تقييم الجنين المعرض لخطر الاصابة بتشوهات الانتروب العصبي، تشكل التشوهات الخلقية برأس وجه الجنين أحد الأسباب الهامة لوفيات الأجنة. وتساعد الموجات فوق الصوتية رياضية الإعداد على التشخيص الدقيق لهذه التشوهات. يهدف هذا البحث إلى تقييم دور الموجات فوق الصوتية رياضية الإعداد في تشخيص التشوهات الخلقية برأس وجه الجنين. تم إجراء هذه الدراسة على 20 سيدة حامل مشكوك في أسباب الاجتهاد عيب خلقية برأس وجه من خلال السونار ثلاثي الأبعاد في مستشفى طنطا الجامعي. وقد تم فحص جميع الحالات بالموجات فوق الصوتية ثلاثية رياضية الإعداد. تم أخذ مساحة كاذبة من جميع المرضى مع احترام خصوصيتهم بعد أظهرت نتائج الدراسة أن سلبية الموجات فوق الصوتية رياضية الإعداد لتشخيص التشوهات الخلقية الخ ما تسرب 94.74% بينما نتائج التشخيص عن طريق الموجات فوق الصوتية رياضية الإعداد تصل إلى 95% بينما تبلغ سلبية ودقة الموجات فوق الصوتية رياضية لتشخيص التشوهات بعظام الوجه 100% وتبلغ حساسية ودقة الموجات فوق الصوتية رياضية لتشخيص التشوهات بوجه الأجنة 100% لذلك تقوفت الموجات فوق الصوتية رياضية الإعداد على الموجات فوق الصوتية ثلاثية الإعداد في تشخيص التشوهات الخلقية برأس وجه الأجنة.