Assessment of Diagnostic Value of 4D Ultrasound in Evaluation of Congenital Fetal Abdominal and Genitourinary Anomalies

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Original Research Article

ABSTRACT

Background: The utilization of three-dimensional (3D) and four-dimensional (4D) ultrasound technology offers supplementary capabilities, such as multiplanar mode, tomographic mode, and surface rendering mode. These additional functionalities contribute to the precise identification and diagnosis of fetal congenital abnormalities. The aim of this was to determine the accuracy of 4D sonography in assessing the congenital fetal abdominal and genito-urinary anomalies of second and third trimesters in high-risk females, compared to the two-dimensional (2D) sonography.

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Methods: The study was carried out on 50 high-risk pregnant women from 20 to 36 weeks with suspected congenital abdominal and genito-urinary anomalies by 2D US and then by 4D US. Data collected from both modalities were evaluated separately using a four-point "Likert scale". The diagnosis was confirmed by postnatal follow-up.

Results: 4D US reported a statistically significant difference in the accuracy/diagnostic confidence in the detection of abdominal & genito-urinary anomalies and in detection of associated fetal congenital anomalies in other body systems as compared to 2D US.

Conclusions: 4D US is a valuable adjunct to 2D US owing to its ability to improve the diagnostic capability of fetal congenital anomalies by offering additional anatomical information through its different display modes.

1. INTRODUCTION

Fetal congenital abnormalities constitute a significant etiological factor in perinatal and newborn death rates, as well as a contributing factor to childhood illness [1]. The utilization of US for prenatal diagnosis of congenital defects is a globally practiced method employed to assess the structural development of the fetus during the entire duration of gestation [2].

The identification of structural defects during the prenatal period offers expectant parents an early chance to acquire knowledge about the condition, encompassing its expected outcome, characteristics, causes and the potential for postnatal or prenatal treatments [3]. In recent years, there has been important development in the field of 4D US technology. This technique has emerged as a valuable tool in routine diagnosis of prenatal , serving as a complementary approach to the conventional two-dimensional (2D) US method [4].

The 4D US exhibits superior image quality compared to the conventional 2D ultrasound, since it enables the visualization of tissue details that are nearly as visible as those shown in Magnetic Resonance (MR) imaging. The most recent technical advancement in medical imaging, known as 4D ultrasound, enables the real-time visualization of three-dimensional (3D) spatial dimensions including width,depth and length on a monitor [5].

The utilization of 4D sonography offers the capability to generate images that are unattainable through 2D US techniques. This advanced technology enables the retention not solely of images, but also of volumetric data that can be afterwards retrieved and subjected to further analysis at any given point in time [4].

The utilization of 4D sonography offers several advantages that contribute to the enhanced evaluation of fetal anomalies detected by 2D sonography. These advantages include nontraditional imaging planes ,expedited acquisition of desired fetal volumes and the ability to employ diverse , the capability to acquire data from remote locations and the potential for offline reconstruction,. These features collectively establish 4D sonography as a valuable complementary tool in the fetal anomalies evaluation [5].

Fetal anomalies can be categorized into two distinct groups. The first group consists of congenital defects that were present earlier in the pregnancy but were not detected despite adherence to first and second trimester screening programs. This lack of detection can be attributed to factors such as unfavorable fetal lie or maternal habitus . The second group encompasses structural abnormalities that develop or become apparent only in late pregnancy. These abnormalities, such as gastrointestinal abnormalities associated with urinary tract abnormalities or intestinal obstruction that may undergo changes over time like dilation of renal pelvis , can only be observed as the fetus matures [6].

Significant morbidity and mortality is still associated with anterior abdominal wall abnormalities such omphalocele, gastroschisis, and bladder exstrophy. The most frequent gastrointestinal abnormalities are esophageal atresia, followed by duodenal atresia, jejunoileal atresia, and anorectal atresia [7]. The differential diagnosis for a cystic abdominal mass in a fetus encompasses a wide range of possibilities, such as ovarian cysts in female fetuses, choledochal cysts, hepatic, splenic, or pancreatic cysts, mesenteric cysts, meconium pseudocyst, adrenal

hemorrhagic cysts, renal cysts, and intestinal duplication cysts [8].

Urinary tract abnormalities include about one-third (33%) of all malformations identified during conventional prenatal sonography. During the prenatal period, many urinary tract abnormalities are often detected, including renal agenesis, renal ectopia, horseshoe kidney, multicystic dysplastic kidney, cystic renal dysplasia with blockage, Autosomal recessive polycystic kidney disease (ARPKD), ADPKD, and hydronephrosis [1]. Ambiguous or Abnormal genitalia may also be observed [7].

Therefore, the use of prenatal diagnostics for the detection of congenital fetal defects enhances the planning process for delivery and facilitates the provision of counseling services [9]. Fetal intervention, if accessible and administered in a suitable manner, has the potential to provide favorable long-lasting effects and enhance postnatal life [1].

The objective of this research was to evaluate the precision of 4D sonography in the evaluation of congenital fetal genitourinary and abdominal defects during the third and seconed trimesters in high-risk pregnant individuals, in contrast to 2D sonography, with a link to postnatal outcomes.

2. METHODS

This investigation was conducted on a cohort of fifty pregnant women who had high-risk pregnancies, specifically those between twenty and thirty-six weeks gestation, and were suspected of having fetal congenital genitourinary and abdominal anomalies. The diagnostic tools used in this research were 2D and 4D ultrasound. The high-risk factors considered for inclusion in the research were consanguineous marriage, advanced maternal age for over thirty-five years, prior history of fetal malformation, positive family history of fetal anomalies, among others. The investigation was conducted between March 2022 and March 2023 subsequent to receiving clearance from the Ethical Committee of Tanta University Hospitals. All patients provided informed written permission.

The exclusion criteria included normal fetal biometry, as well as deadly congenital abnormalities such as hypoplastic left heart syndrome anencephaly and encephalocele . Additionally, pregnant women with significant oligohydramnios were also excluded from the research.

All participants had a comprehensive assessment, which included obtaining their medical history as well as doing 2D and 4D examinations of ultrasound.

2.1 Two-Dimensional (2D) US Examination

All patients were initially scanned by two-dimensional trans-abdominal probe using a Samsung HS50 ultrasound equipment and TOSHIBA Aplio 500 ultrasound equipment with a convex abdominal transducer (3-5 MHz), the 2D US scan was used to identify &localize the region of interest; the fetal internal abdominal organs, urinary system & genitalia.

While applying minimal pressure on the patient's abdomen, the depth, sector width, and focal zone of the area of interest were adjusted. The area was magnified by selecting the "zoom" option on the ultrasound machine either by zooming the whole image or selecting an area of interest from the image to magnify. Basic examination of the fetal abdomen in addition to examination of urinary & genital systems; in axial, sagittal, and coronal planes to demonstrate detailed anatomy of the fetal abdominal & genitourinary organs.

2.2 4D US Examination

Following the first identification of a potential abdominal or genitourinary defect during the 2D examination, a further 4D examination was conducted with a 4D trans-abdominal transducer in order to acquire an ultrasonic volume. The process of capturing a picture for each patient in 4D mode was executed via the following sequential phases:

1. To begin the examination process, please proceed by selecting the 4D button on the keyboard or accessing the 4D live option within the alternative menu shown on the touch panel.
2. Setting the ROI by moving the cursor to the function icon and changing the function assigned to the trackball by pressing SET or NEXT.
3. Adjusting the ROI size by (a) pressing EDIT ROI in the Volume menu on the touch panel, (b) operating the trackball to adjust the ROI size, or (c) pressing the set button.
4. Adjusting the flexible cut line by (a) pressing the flexible cutline in the volume menu on the touch panel or (b) operating

the trackball to adjust the position of the flexible cut line (plane A).

5. Activating the 4D function or accessing the 4D live feature inside the alternative menu shown on the touch screen.

The duration of the 4D examination ranged from 15 to 20 minutes. In conclusion, the examination's saved images may be observed in 4D mode by using the patient browser button. This involves navigating through the main menu, selecting the 4D data option, and then choosing the view option from the touch screen interface. Only images with an acceptable quality of the abdomen & genitalia were included in the research that allowed visualization of the internal abdominal organs including the stomach,urinary bladder ,external genitalia and kidneys. Any other associated anomalies including fetal lips, CNS,skeletal or cardiovascular systems detected during the examination were also recorded by both 2D & 4D images. Fetal abnormalities that were identified were digitally archived on a disk and documented in writing form.

2.3 Outcome Measures

Most cases were followed up postnatally either clinically or by an imaging modality (such as ultrasonography, X-ray, computerized tomography (CT), MRI, surgery, or pathology). Data collected from 2D & 4D examinations were evaluated separately using a four-point "Likert scale" [10], The diagnostic confidence in recognizing particular anomalies is assessed on a scale ranging from one to four, the clarity of the distinction. The levels of confidence in postnatal correlation among completed or preterm pregnancies may be categorized as follows: not confident (or uncertain), at least fairly confident, and confident. Post-natal data was considered the golden standard for the accuracy of prenatal 2D & 4D US findings.

2.4 Statistical Analysis

The statistical analysis was conducted using SPSS v26, a software developed by IBM Inc. in Chicago, IL, USA. The normality of the data distribution was assessed using histograms and the Shapiro-Wilks test. The data given in this research were parametric and quantitative in nature, and were summarized using the standard deviation (SD) and average. The data given in this research were non-parametric and quantitative and were summarized using the interquartile range (IQR) and median. The

presentation of qualitative variables was done in the form of percentage and frequency (%).

3. RESULTS

According to maternal demographic data, seventeen cases (34%) were primigravida & thirty three cases (66%) were multigravida. fourteen cases (28 %) have a positive history of consanguinity. The maternal age with Average ± SD = 28.72 ± 3.80. twelve cases (24%) were hypertensive, twelve cases (24%) were diabetic, eight cases (16%) were anaemic, seven cases (14%) were obese. There were four cases (8%) with a family history of fetal congenital anomalies. There were eight cases (16%) with a previous history of fetal malformation. As regards the history of fetal loss; there were three cases (6%) with previous intrauterine fetal death, five cases (10%) with recurrent abortion & two cases (4%) still birth. three cases (6%) showed a positive drug history. There were four cases (8%) showed elevated amniotic fluid with amniotic fluid index (AFI) more than twenty five, eight cases (16%) showed decreased amniotic fluid with AFI less than five and thirty eight cases (76 %) showed average amount of amniotic fluid Table 1.

According to fetal gender, twenty nine fetuses (58%) were males, twenty fetuses (40%) were females, and one fetus (2%) was intersex. Mean (± SD) of the gestational age was 24.04 (± 3.06). seven anomalies (14%) were omphalocele, three anomalies (6%) were gastroschisis, two anomalies (4%) were duodenal atresia, one anomaly (2%) was liver calcification, two anomalies (4%) were ascites / AC high, one anomaly (2%) was a choledochal cyst. As regards urinary anomalies; ten anomalies (20%) were pyelectasis/ hydronephrosis/ PUJ obstruction, six anomalies (12%) were multicystic dysplastic kidney, ten anomalies (20%) were ARPKD, three anomalies (6%) were renal agenesis, and one anomaly (2%) was a simple renal cyst. As regard the genital system anomalies, one anomaly (2%) was an ovarian cyst & one anomaly (2%) was ambiguous genitalia. There were two cases showed mixed abdominal & renal anomalies, one anomaly (2%) was a posterior urethral valve with bilateral hydro-uretro-nephrosis and one case (2%) was cloacal exstrophy with left hydronephrosis and right renal agenesis. Table 2.

Out of 50 cases, there were 15 cases (30%) showed associated anomalies either CNS,

cardiac or skeletal anomalies. There was 1 associated anomaly (2%) identified as myelomeningocele, 1 anomaly (2%) was meningocele, 2 anomalies (4%) were hydrocephalous, 1 anomaly (2 %) was spinal dysraphism, 1 anomaly (2%) was occipital meningocele, 1 anomaly (2%) was cystic hygroma & 3 anomalies (6%) were cleft lip.2 associated anomalies (4%) were VSD &1 anomaly (2%) was pericardial effusion. 5 associated anomalies (10%) were club foot, 1 anomaly (2%) was arthrogryposis, and 1 associated anomaly (2%) was polydactyly. As regards those 15 cases, each case showed one associated anomaly except 3 cases, one of them showed 2 associated anomalies (pericardial effusion & club foot) and 2 cases showed 3 associated anomalies, one of them was (Arthrogryposis, club foot, & VSD) and the other one was (Occipital meningocele, cleft lip & spinal dysraphism). 2 cases (4%) underwent termination of pregnancy, 4 cases (8%) were still-birth, 12 cases (24%) were preterm live babies & 32 cases (64%) were born as term live babies Table 3.

As regards abdominal anomalies, Omphalocele (7 cases), by 2D US (2 cases (4%) were mildly confident and 5 cases (10%) were moderately confident). By 4D ultrasound, all cases were confident. Gastroschisis (3 cases) (6%), by 2D US were mildly confident. By 4D ultrasound were confident. Choleducal cyst (1 case) (2%), by 2DUS was confident. By 4D US was mildly confident). Ascites/AC high (2 cases) (4%), by 2D US were confident. By 4D US were moderately confident). Liver calcification (1 case) (2%), by 2D US was confident. By 4D US was moderately confident). Duodenal atresia (2 cases) (4%) was confident by both 2D & 4D ultrasounds. As regards renal and urinary tract anomalies, Pyelecatasis/ Hydronephrosis/ PUJ obstruction (10 cases), by 2D US (1 case (2 %) was non-confident, 2 cases (4%) were moderately confident, and 7 cases (14%) were confident). By 4D US(10 cases (20%) were confident). Multicystic dysplastic kidney (6 cases) (12%), by 2D US (1 case (2%) was moderately confident & 5 cases (10%) were confident). By 4D US, all cases were moderately confident. ARPKD (10 cases) by 2D US (2 cases (4%) were moderately

Table 1. The table is demonstrated that distribution of the studied cases according to , maternal comorbidities, family history, history of fetal malformation maternal ,demographic data & loss, maternal drug history and liquor /Amniotic fluid (n = fifty)

		No.	%
Maternal demographic data			
Parity/gravid	Primigravida	seventeen	34.0
	Multigravida	Thirty three	66.0
Consanguinity	Negative	Thirty six	72.0
	Positive	Thirty six	28.0
Age of mother (years)		28.72 ± 3.80	
Maternal comorbidities			
Hypertension		twelve	24.0
DM		twelve	24.0
Anemia		eight	16.0
Obese (BMI > 30)		seven	14.0
No maternal comorbidities		eleven	22.0
Family history			
Fetal congenital anomalies		four	8.0
Past history of fetal malformation & loss			
Previous history of fetal malformation		eight	16.0
Fetal loss	Previous intrauterine fetal death	three	6.0
	Recurrent abortion	five	10.0
	Still birth	two	4.0
Drug history		three	6.0
Liquor /Amniotic fluid			
Poly		four	8.0
Oligo		eight	16.0
Average		Thirty eight	76.0

Data are demonstrated as number (%) or average± SD. DM: diabetes mellites. BMI: body mass index

Table 2. Distribution of the studied cases according to the gestational age and sex of the fetus , genitourinary and abdominal anomalies (n = 50)

	No.	%
Gender of fetus		
Male	29	58.0
Female	20	40.0
Intersex	1	2.0
Gestational age (weeks)	24.04 ± 3.06	
Abdominal anomalies		
Omphalocele	7	14.0
Gastroschisis	3	6.0
Duodenal atresia	2	4.0
Liver calcification	1	2.0
Ascites / AC high	2	4.0
Choledochal cyst	1	2.0
Urinary anomalies		
Pyelectasis/ Hydronephrosis/ PUJ obstruction	10	20.0
Multicystic dysplastic kidney	6	12.0
ARPKD	10	20.0
Renal agenesis	3	6.0%
Simple renal cyst	1	2.0
Genital system anomalies		
Ovarian cyst	1	2.0
Ambiguous genitalia	1	2.0
Mixed abdominal and urinary system anomalies		
Posterior uretheral valve with bilateral hydrouretronephrosis	1	2.0
Cloacal exstrophy with left hydronephrosis and right renal agenesis	1	2.0

Data are presented as number (%) or mean ± SD. AC: ascites in cirrhosis. PUJ: Pelvi-ureteric junction. ARPKD: Autosomal recessive polycystic kidney disease

confident & 8 cases (16%) were confident). By 4D US (1 case (2%) was moderately confident and 9 cases (18%) were confident). Renal agenesis (3 cases), by 2D US (1 case (2%) was mildly confident, 1 case (2%) was moderately confident & 1 case (2%) was confident). By 4DUS (1 case (2%) was moderately confident & 2 cases (4%) were confident). As regards, posterior urethral valve with bilateral hydrouretronephrosis (1 case (2%) was confident by both 2D & 4D USs. Also, Simple renal cyst (1 case (2%) was confident by both 2D & 4D ultrasounds. Regarding genital system, Ovarian cyst (1 case (2%) was confident by both 2D & 4D ultrasounds. Ambiguous genitalia (1 case (2%)) by 2D ultrasound, was moderately confident & by 4D US was confident). As regards mixed abdominal & urinary anomalies cases, Cloacal exstrophy with left hydronephrosis & right renal agenesis (1 case (2%) was moderately confident by 2D US& by 4D USwas confident). Table 4.

Based on assessment of associated anomalies of other body systems by "Likert scale ", the diagnostic confidence (accuracy) of both 2D and 4D ultrasounds was evaluated .As regards, Meningocele (1 case (5%), Myelomeningocele (1 case (5%), Spinal dysraphism (1 case (5%), Occipital meningocele (1 case (5%), Cystic hygroma (1 case (5%) and Arthrogryposis (1 case (5%), by 2D US were moderately confident. By 4D ultrasound, were all confident. Hydrocephalous (2 cases (10%), Polydactyly (1 case (5%) & Pericardial effusion (1 case (5%) were confident by both 2D &4D ultrasounds. Cleft lip (3 cases), by 2D ultrasound; (2 cases (10%) were mildly confident & 1 case (5%) was moderately confident). By 4D ultrasound, (3 cases (15%) were confident). As regards, VSD (2 cases) (10%), by 2D ultrasound; (1 case (5%) was moderately confident & 1 case (5%) was confident). By 4D ultrasound, both were confident. Club foot (5 cases) by 2D ultrasound; (3 cases (15%) were moderately confident & 2 cases (10%) were confident). By 4D ultrasound, (1 case (5%) was moderately confident & 4 cases (20%) were confident). Table 5.

Table 3. Distribution of the studied cases according to associated anomalies of other body systems (n= 15 cases) & (n=20 associated anomalies) and post-natal fate (n=50)

		No.	%
Associated anomalies			
No associated anomalies		35	70.0
With associated anomalies		15	30.0
Neural tube defects (CNS) anomalies	Myelomeningocele	1	2.0
	Meningocele	1	2.0
	Hydrocephalous	2	4.0
	Spinal dysraphism	1	2.0
	Occipital meningocele	1	2.0
	Cystic hygroma	1	2.0
	Cleft lip	3	6.0
Cardiac anomalies	VSD	2	4.0
	Pericardial effusion	1	2.0
Skeletal anomalies	Club foot	5	10.0
	Arthrogryposis	1	2.0
	Polydactyly	1	2.0
Post-natal fate			
Termination of pregnancy		2	4.0
Still-birth		4	8.0
Preterm live baby		12	24.0
Term live baby		32	64.0

Data are presented as number (%). CNS: central nervous system. VSD: Ventricular septal defect.

Table 4. Distribution of the studied cases according to accuracy (Diagnostic confidence) of abdominal and genito-urinary anomalies (n=50 cases)

Diagnostic confidence	2D		4D	
	No.	%	No.	%
Omphalocele				
Non- confident (1)	0	0.0	0	0.0
Mildly confident (2)	2	4.0	0	0.0
Moderately confident (3)	5	10.0	0	0.0
Confident (4)	0	0.0	7	14.0
Gastroschisis				
Non confident (1)	0	0.0	0	0.0
Mildly confident (2)	3	6.0	0	0.0
Moderately confident (3)	0	0.0	0	0.0
Confident (4)	0	0.0	3	6.0
Choleducal cyst				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	1	2.0
Moderately confident (3)	0	0.0	0	0.0
Confident (4)	1	2.0	0	0.0
Ascites/ AC high				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	0	0.0	2	4.0
Confident (4)	2	4.0	0	0.0
liver calcification				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0

Diagnostic confidence	2D		4D	
	No.	%	No.	%
Moderately confident (3)	0	0.0	1	2.0
Confident (4)	1	2.0	0	0.0
Duodenal atresia				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	0	0.0	0	0.0
Confident (4)	2	4.0	2	4.0
Pyelecatasis/ Hydronephrosis/ (PUJ) obstruction				
Non confident (1)	1	2.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	2	4.0	0	0.0
Confident (4)	7	14.0	10	20.0
Multicystic dysplastic kidney				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	1	2.0	0	0.0
Confident (4)	5	10.0	6	12.0
ARPKD				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	2	4.0	1	2.0
Confident (4)	8	16.0	9	18.0
Renal agensesis				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	1	2.0	0	0.0
Moderately confident (3)	1	2.0	1	2.0
Confident (4)	1	2.0	2	4.0
Posterior uretheral valve with bilateral hydrouretronephrosis				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	0	0.0	0	0.0
Confident (4)	1	2.0	1	2.0
Renal cyst				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	0	0.0	0	0.0
Confident (4)	1	2.0	1	2.0
Ovarian cyst				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	0	0.0	0	0.0
Confident (4)	1	2.0	1	2.0
Ambiguous genitalia				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	1	2.0	0	0.0
Confident (4)	0	00	1	2.0
Cloacal exstrophy with left hydronephrosis & right renal agenesis				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	1	2.0	0	0.0
Confident (4)	0	0.0	1	2.0

Data are presented as number (%). AC: ascites in cirrhosis. PUJ: Pelvi-ureteric junction. ARPKD: Autosomal recessive polycystic kidney disease.

Table 5. Distribution of the studied cases according to accuracy (Diagnostic confidence) of associated anomalies of other body systems

Associated anomalies	2D		4D	
	No.	%	No.	%
Meningocele				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	1	5.0	0	0.0
Confident (4)	0	0.0	1	5.0
Myelomeningeocle				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	1	5.0	0	0.0
Confident (4)	0	0.0	1	5.0
Hydrocephalous				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	0	0.0	0	0.0
Confident (4)	2	10.0	2	10.0
Spinal dysraphism				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	1	5.0	0	0.0
Confident (4)	0	0.0	1	5.0
Occipital menigeocele				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	1	5.0	0	0.0
Confident (4)	0	0.0	1	5.0
Cystic hygroma				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	1	5.0	0	0.0
Confident (4)	0	0.0	1	5.0
Cleft lip				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	2	10.0	0	0.0
Moderately confident (3)	1	5.0	0	0.0
Confident (4)	0	0.0	3	15.0
VSD				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	1	5.0	0	0.0
Confident (4)	1	5.0	2	10.0
Pericardial effusion				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	0	0.0	0	0.0
Confident (4)	1	5.0	1	5.0
Club foot				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0

Associated anomalies	2D		4D	
	No.	%	No.	%
Moderately confident (3)	3	15.0	1	5.0
Confident (4)	2	10.0	4	20.0
Polydactyly				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	0	0.0	0	0.0
Confident (4)	1	5.0	1	5.0
Arthrogryposis				
Non-confident (1)	0	0.0	0	0.0
Mildly confident (2)	0	0.0	0	0.0
Moderately confident (3)	1	5.0	0	0.0
Confident (4)	0	0.0	1	5.0

Data are presented as number (%). VSD: Ventricular septal defect. 4D,. 2D: ultrasound compared to two-dimensional

There was a statistically significant difference in the accuracy/diagnostic confidence of 4D ultrasound compared to 2D ultrasound regarding the detection of abdominal & genito-urinary anomalies and in detection of associated fetal congenital anomalies in other body systems such as craniofacial, cardiac and skeletal systems. Table 6.

Out of 2 cases who underwent termination of pregnancy, one anomaly (50%) was ascites with associated VSD, arthrogryposis and club foot and the other (50%) was cloacal exstrophy with left hydronephrosis & right renal agenesis and club foot. 1 anomaly (25%) was omphalocele with cystic hygroma, 1 anomaly (25%) was multicystic dysplastic kidney, 1 anomaly (25%) was ARPKD with meningocele & 1 anomaly (25%) was bilateral renal agenesis. Out of 12 cases of preterm babies, 2 anomalies (16.7%) were omphalocele, 1 anomaly (8.3%) was gastroschisis, 1 anomaly (8.3%) was ascites, 1 anomaly (8.3%) was duodenal atresia, 3 anomalies (25%) were multicystic dysplastic kidney, 3 anomalies (25%) were ARPKD & 1 anomaly (8.3 %) was ambiguous genitalia Table 7.

The sensitivity of 2D ultrasound for detection of fetal abdominal & genito-urinary anomalies was (95 %), the specificity of 2D in fetal abdominal & genito-urinary anomalies was (100%), PPV= (100 %), NPV= (66.67%) & accuracy = (95.45%). As regard to abdominal & genito-urinary anomalies, the sensitivity of 4D ultrasound for detection of fetal abdominal & genito-urinary anomalies was (97.50 %), the specificity of 4D in fetal abdominal & genito-urinary anomalies was (100%), PPV= (100 %), NPV= (80 %) & accuracy = (97.73 %). Table 8.

Table 6. Comparison between 2D and 4D according to accuracy (Diagnostic confidence (n=50 cases) of fetal congenital abdominal & genito-urinary anomalies and associated anomalies (n=20 anomalies)

	2D (n =50)		4D (n= 50)		MH	p
	No.	%	No.	%		
Diagnostic confidence						
Non-confident	1	2.0	0	0.0	82.0[*]	0.004[*]
Mildly confident (2)	6	12.0	1	2.0		
Moderately confident (3)	13	26.0	5	10.0		
Confident (4)	30	60.0	45	90.0		
Associated anomalies						
Non-confident (1)	0	0.0	0	0.0	41.0[*]	0.001[*]
Mildly confident (2)	2	10.0	0	0.0		
Moderately confident (3)	11	55.0	1	5.0		
Confident (4)	7	35.0	19	95.0		

Data are presented as number (%).MH: Marginal Homogeneity Test. p: p value for comparison between 2D and 4D

Table 7. Relation between diagnosis & post-natal fate

Diagnosis	Post-natal fate							
	Termination (n = 2)		Still birth (n = 4)		Preterm live baby (n = 12)		Term live baby (n=32)	
	No.	%	No.	%	No.	%	No.	%
Omphalocele	0	0.0	1	25.0	2	16.7	4	17.4
Gastroschisis	0	0.0	0	0.0	1	8.3	2	6.25
Ascites/ AC high	1	50.0	0	0.0	1	8.3	0	0.0
Liver calcification	0	0.0	0	0.0	0	0.0	1	3.12
Duodenal atresia	0	0.0	0	0.0	1	8.3	1	3..12
Choledochal cyst	0	0.0	0	0.0	0	0.0	1	3.12
Pyelecatasis/ Hydronephrosis / PUJ obstruction	0	0.0	0	0.0	0	0.0	10	31.25
Multicystic dysplastic kidney	0	0.0	1	25.0	3	25.0	2	6.25
ARPKD	0	0.0	1	25.0	3	25.0	6	18.75
Renal agenesis	0	0.0	1	25.0	0	0.0	2	6.25
Posterior urethral valve	0	0.0	0	0.0	0	0.0	1	3.12
Simple renal cyst	0	0.0	0	0.0	0	0.0	1	3.12
Ovarian cyst	0	0.0	0	0.0	0	0.0	1	3.12
Ambiguous genitalia	0	0.0	0	0.0	1	8.3	0	0.0
Cloacal exstrophy with left hydronephrosis & right renal agenesis	1	50.0	0	0.0	0	0.0	0	0.0

Data are presented as number (%). PUJ: Pelvi-ureteric junction. ARPKD: Autosomal recessive polycystic kidney disease

Table 8. Agreement (sensitivity, specificity and accuracy) for abdominal and genitourinary anomalies for 2D and 4D USs

|	Post natal				Sensitivity	Specificity	PPV	NPV	Accuracy
	Negative (n = 4)		Positive (n = 40)						
	No.	%	No.	%					
2D									
Negative	4	100.0	2	5.0	95.0	100.0	100.0	66.67	95.45
Positive	0	0.0	38	95.0					
4D									
Negative	4	100.0	1	2.5	97.50	100.0	100.0	80.0	97.73
Positive	0	0.0	39	97.5					

*Data are presented as number (%).4D, 2D: ultrasound compared to two-dimensional. P: p value for association between different categories. *: Statistically significant at p ≤ 0.05. PPV: Positive predictive value NPV: Negative predictive value*

3.1 Case 1

A pregnant female aged 25 years, primigravida, hypertensive, with a positive history of consanguinity, presented at 20 weeks of gestation with a female fetus, was referred for an anomaly scan with unremarkable prior antenatal check-ups. Diagnosis: A case of Gastroschisis. Fig. 1.

3.2 Case 2

A pregnant female aged 26 years, Multigravida, diabetic, with negative family and consanguinity history, presented with a male fetus at 22 weeks of gestation. She was referred for a routine antenatal check-up & anomaly scan. Diagnosis: A case of right pyelectasis Fig. 2.
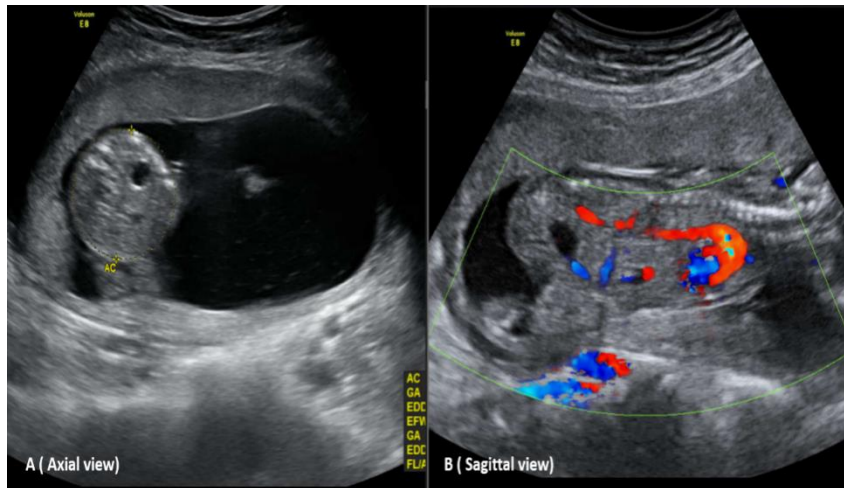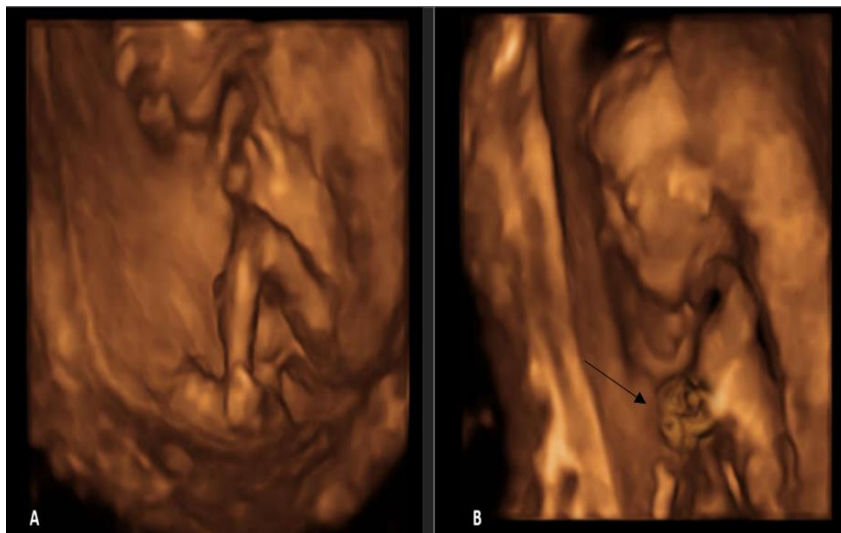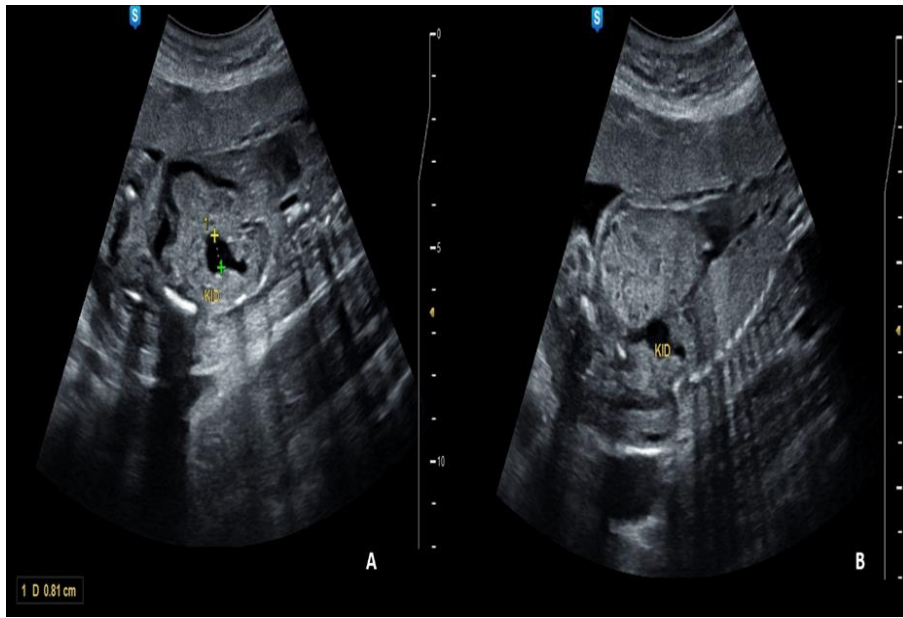
Fig. 1. I) 2D ultrasound images (A): axial view, (B): sagittal view are demonstrating fetal anterior abdominal wall defect with protrusion of the bowel loops out the abdominal cavity without any covering and II) (A & B) images demonstrate surface rendering 4D US images of the fetal abdomen with free-floating herniated bowel

4. DISCUSSION

The use of 4D US technology has facilitated the assessment of intricate anatomical features via the application of a multiplanar method. Additionally, it has allowed for the estimation of fetal organ volumes utilizing virtual organ computer-aided analysis techniques. Furthermore, the tomographic approach may be used to reformat anatomical features, while the rendering technique known as HD-live can be utilized for surface examination of tiny faults [11].

In the current study, 66% of women were multigravida which matched with the results of Qadir et al, [12] where the majority of cases; 66 cases (56.4%) were multigravida. This may be attributed to the fact that the rate of multiparty is still increasing in developing countries while in developed countries is becoming low [13]. On the other hand, Nowlan NC, [14] found that with the primigravida, the first fetus might initially distend the uterus and the abdminal wall as the uterus is more resistant to stretch. Thus, the first born infant usually experiences more constraint and more chances for fetal deformities.

I
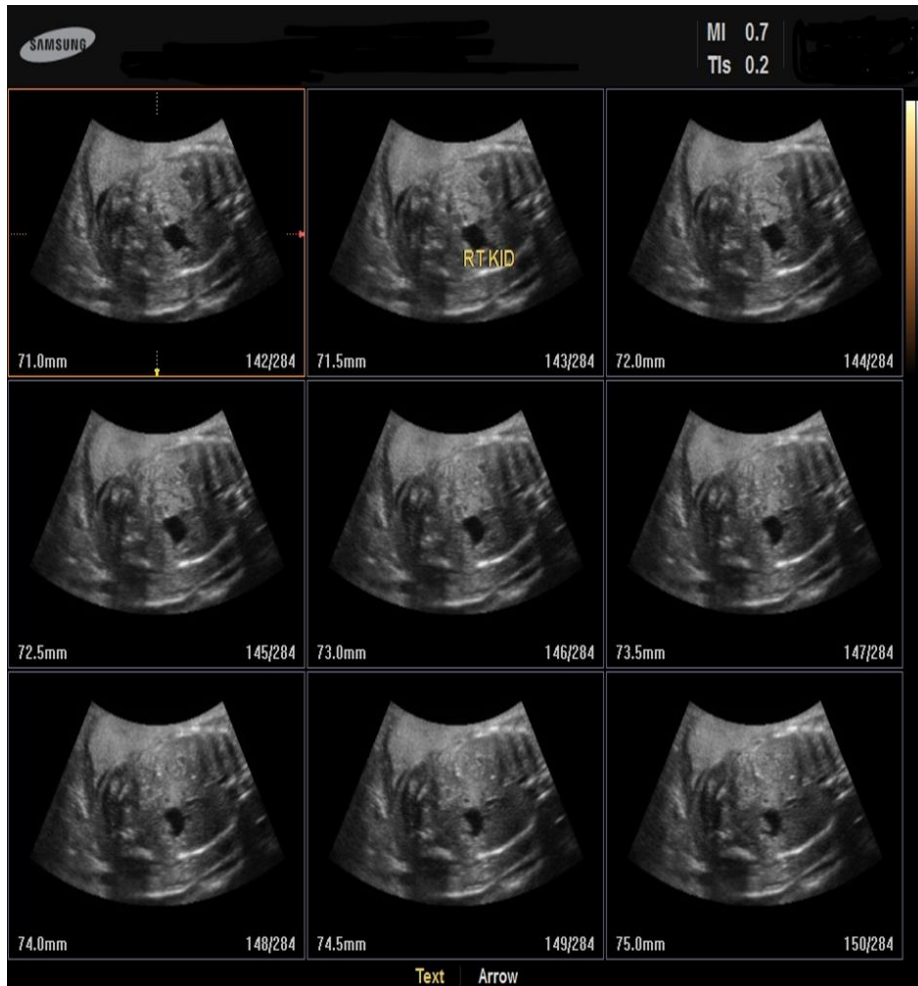
II

III

Fig. 2. Case 2 showed that: I) (A& B): sagittal view of 2D ultrasound images are demonstrating echogenic right fetal kidney with moderate dilation of antero-posterior renal pelvic diameter measuring about 8 mm with normal left kidney, II) the sagittal view of Tomographic ultrasound images (TUI) of the right fetal kidney with dilated AP diameter, with slice thickness 5mm and III) postnatal US examination

Regarding the history of consanguinity, only 28% of cases had a positive history of consanguinity. This matched with Patil et al , [15] who showed that there was no significant difference (p>0.05) in the number of congenital malformations between the consanguineous and non-consanguineous groups. This lower incidence of consanguinity in our study may be explained as the frequency of consanguineous marriage is generally declining nowadays due to increased awareness of its hazards especially among urban population [16].

On contrary, Ben-Omran et al, [17] proved that consanguinity plays an important role in the occurrence of congenital anomalies.

Regarding the maternal age, in the current study, the mother's age ranged from 19 to 36 years with mean of 28.72 ± 3.80(± SD) years which was in accordance with the study made by Zvizdic et al, [18] in which the mean of (±SD) maternal age of infants with congenital anomalies was 27.8 ± 4.2(SD) years. It was suggested that the increase in age brings with it many other chronic diseases in the mother which affect her state of immunity and impair her withstanding abilities and the non-disjunction and mutations [19].

On the other hand, Ahn et al, [20] found that in young mothers, the incidence of having children with abdominal wall defects and oral cleft/ lip defects was significantly increased.

Regarding the risk factors as maternal comorbidities including hypertension, in the current study, 24% of mothers had experienced either chronic hypertension or pregnancy-induced hypertension and this agreed with Demir et al , [21]. The study shown that the occurrence rate of significant congenital abnormalities among 8,307 women with managed chronic hypertension was 5.9%, in contrast to the 3.5% rate seen in the general population of women without chronic hypertension.

On the other hand, a study by Un Nisa et al , [22] proved that there were no complications seen in the babies of mothers with chronic hypertension and superimposed-pregnancy hypertension.

As regards DM, in the present study, 24% of cases were diabetic. This agreed with a study

conducted by Dart et al , [23] on 945 infants with congenital anomalies of the kidney and urinary tract (CAKUT), that GDM was from the most significant factors which affects the fetal genitourinary system(P value < 0.001).

On contrary, Wu et al, [24] proved that maternal GDM was inversely associated with the risk of gastroschisis and anencephaly for currently unkonwn reasons.

As regards maternal anemia, in our study, 16% of mothers were found to be anemic (Hb less than 10 g/dl). This was in accordance with a study by Rehan et al, [25] which revealed that amongst 12,400 patients, 2211(17.8%) were found to have Hb =10 g/dl while 5064 (41.3%) patients were found to have Hb less than 10 g/dl and thus there was a high association between folic acid deficiency and fetal congenital CNS and genitourinary anomalies as hypospadias and bladder outlet obstruction.

Regarding maternal obesity, in the current study, 14% of women were having BMI > 30 and were not suffering from any other chronic comorbidities. This agreed with Moraes CL De , [26] who found that out of 53 babies with genitourinary anomalies , 6 mothers (11.32%) were obese and 10 mothers (18.87%) were overweight (BMI> 40).

As regards the family history of fetal anomalies, only 8% of cases in our study showed positive family history of fetal malformations. This was consistent with Mekonnen et al, [27].who found that only 10 cases (7.4%) out of 160 cases reported a family history of anomalies. On the other hand, Qu et al, [28] stated that a family history of birth defects has been associated with an increased recurrence risk of congenital anomalies.

Regarding the past history of fetal malformations, in the current study, only 16% of mothers experienced previous history of fetal malformations. This matched with a study conducted by Kumar Samal et al, [29] who found that only 7 cases (5%) out of 140 cases had a previous history of fetal anomaly.

This slight lower incidence of assoissation between the previous history of fetal malformations and fetal congenital anomalies in our study may owe to the fact of increasing maternal care during pregnancy and awareness of maternal follow up.

On contrary, Ameen et al, [30] showed that there was a statistically significant association between having a child with congenital anomalies and a maternal history of previous congenital anomalies .

Regarding the history of previous fetal loss, in the current study; there were 6% of mothers with previous intrauterine fetal death in cases of hydronephrosis, multicystic dysplastic kidney and ambigious genitalia, 10% suffered from recurrent abortion in 2 cases of gastroschisis, 1 case of omphalocele, 1 case of ARPKD & 1 case of cloacal exstrophy & 4% had a history of stillbirth in cases of duodenal atresia & renal agenesis.

This was in coordinace with Campaña et al, [31] The individual(s) responsible for establishing the correlation between women who have had prior miscarriages and an elevated likelihood of developing five specific birth abnormalities, namely gastroschisis, omphalocele, talipes equinovarus, spina bifida, and hypospadias, have not been explicitly mentioned in the provided text.

Regarding the drug history, only 6% of women revealed a positive drug history this was similar to a study by Jiang et al , [32] who stated that there was no statistically significant difference for maternal history of medication during pregnancy between the infants with CAKUT and those without CAKUT. While Taye et al, [33] proved that unidentified medication use during early pregnancy had a significant association with the occurrence of fetal congenital anomalies.

As regards the amniotic fluid volume, in the present study, 76% of women showed an average amount of amniotic fluid, 16% of women had oligohydramnios in 2 cases of hydronephrosis, 3 cases of ARPKD, 2 cases of multicystic dysplastic kidney and 1 case of bilateral renal agenesis, 8% of women had polyhydramnios in 1 case of hydronephrosis, 2 cases of hydrops fetalis and 1 case of ovarian cyst.

This matched with Nassr et al , [34] who found that 78% of fetuses diagnosed prenatally with lower urinary tract obstruction were associated with a normal volume of amniotic fluid at mid-gestation and had a favorable outcome in terms of perinatal survival but few will need long-term respiratory support.

Regarding the gender of the baby, in our study, 58% were males, 40% were females and 2%

was intersex. This matched with a study by Ara et al, [35]who stated that the overall incidence of congenital anomalies in males was slightly higher than females 34.1/1000 live births and 33.3/1000 live births respectively. Also, Oyinloye et al, [36] found that gastroschisis was slightly higher in males with a male-female ratio of 3.5:1.

This was in contrast with a study by Arfaksad et al, [37] who found that out of 87 fetuses with different congenital anomalies; 47 cases were female fetuses, 34 fetuses were male, and 6 had no clear gender identification. Meanwhile, Khorsheed, et al, [38] revealed that there was no statistical relationship between the sex of the baby and developing fetal abnormalities.

In the present study, the anomalies were noted in the second trimester of gestational age. This agreed with Khanal et al, [39] who found that as regards the gestational age, 11 (10.4%) anomalies were detected at first trimester, 87 (82.1%) in the second trimester and 8 (7.5%) in the third trimester of pregnancy.

In the current study, among the fetal congenital abdominal anomalies, fetal urinary tract anomalies (31 cases) were the most common. Among the urinary anomalies, hydronephrosis/ pyelectasis/ PUJ obstruction (20%) and ARPKD (20%) were the most detected anomalies. These findings were consistent with a study of fetal abdominal anomalies by Kaur, et al, [40] in which hydronephrosis (43.75%) was found to be the most common detected urinary anomaly.

Regarding the diagnostic value of 4D ultrasound, the present study revealed that there was a statistically significant difference between diagnostic confidence of 4D US compared to 2D ultrasound in detection of abdominal & genito-urinary abnormalities and that 4D added more information to 2D ultrasound.in the diagnosis of these abnormalities. The accuracy of 4D US in detection of those anomalies was 97.73 % while the accuracy of 2D US in their detection was 95.45 %. Also, as regards the efficacy of 4D US in detection of anomalies of other body systems including the cranio-facial, cardiac and skeletal systems, and the 4D US showed a statistically significant difference than 2D US in the diagnostic confidence of detection of these abnormalities.

This agreed with a comparative study between 2D and 4D US by Wataganara et al, [41] which

proved 4D US to be advantageous in 60.8% of the defects.

In the research of Öcal et al, [42] proved that as regards the superficial anomalies, 31 cases (49 %) were better visualized with 4D ultrasound, 11 cases (19.7 %) were better visualized with 2D USG, and 19 (31.1 %) were similarly visualized with both methods, 4D US was superior to 2D US in terms of image quality, clarity, the distinction between surrounding structures especially in superficial anomalies.

Regarding the different modes of 4D ultrasound, the surface rendering confirmed the diagnosis in cases of anterior abdominal wall defects as in 7 cases of omphalocele, 3 cases of gastroschisis, 1 case of ambiguous genitalia and 1 case of colacal exstrophy. Also were used in 10 cases of ARPKD, 6 cases of multicystic dysplastic kidney, 1 case of renal cyst, 1 case of psoetrior urethral valve and 1 case of duodenal atresia.

Sadek, [43] stated that despite surface-rendering mode was initially applied on the evaluation of facial and limb anomalies.

Tomographic US mode was used to examine fetal kidneys in 10 cases of pyelectasis and hydronephrosis, 3 cases of renal agenesis and any case associated with cranio-facial anomaly. This came in accordance with Mercé, et al, [44],who revealed that 92 % (2583/2800) of the fetal anatomic structures were correctly identified by multiplanar navigation and TUI and thus, the use of TUI improved identification of fetal anatomic structures in 35% of fetuses.

Considering inversion mode, it was used in the current study to define the course of the dilated parts of the urinary system in cases of simple renal cyst and multicystic dysplastic kidney. Adel, et al, [45] used inversion recovery mode in a study of fetal causes of oligohydramnios to detect the distended urinary bladder & urethra in cases of posterior urethral valve obstruction.

On the other hand, Sadek, [43] revealed in a study on five hundred and sixty five fetuses (503 singleton and 31 pairs of twins) with a total of 776 confirmed malformations that despite the use of different modes of 4D US ,there were no additional information obtained by 4D US regarding neck, thoracic and abdominal malformations.

As regards, the detected associated CNS anomalies (20%), we found that 4D ultrasound is more accurate and has more diagnostic confidence than 2D US in detecting brain abnormalities (P=0.001) which agreed with Abozaid, et al, [46] who found that 3D/4D is more accurate, sensitive and specific, and tend to detect brain anomalies earlier in time than 2D.

However, this disagreed with Hata et al, [47] who stated that the characteristic findings such as the absence of the skull and other brain anomalies by 2D and 3D US were equally detected.

Regarding the detected CVS anomalies (6%), the 4D US was found to be a statistically significant in diagnostic confidence of detection of CVS anomalies than 2D US(P=0.001). This matched with a study by Karmegaraj et al, [48] which proved that the accuracy of prenatal interpretation of detected cardiac anomalies was significantly higher using 3D/4D Spatio-temporal image correlation (STIC) than using 2D US fetal echocardiography.

On the other hand, Yagel et al, [49] revealed that overall 3D/4D US modalities had added value in only about 6% of cases of fetal anatomical CVS anomalies.

In the present research, as regards fetal spinal, upper and lower extremities anomalies (14%), the 4D US was more accurate than 2D US in the detection of these anomalies (P=0.001). Yousef, et al, [50] also found that 4D US is more advantageous in anomalies of the face and extremities only.

Regarding the postnatal fate, the current study showed that the 2 cases (4%) who underwent termination of pregnancy (TOP) were ascites (hydrops) with associated VSD, arthrogryposis and club foot and & the second case was colacal exstrophy with left hydronephrosis & right renal agenesis and the 4 cases (8%) who were born as stillbirth were ARPKD with meningocele, bilateral renal agenesis. multicystic dysplastic kidney and omphalocele with cystic hygroma. In a study by Catania et al, [51] The study shown that the identification of fetal ascites prior to the 24th week of gestation was linked to a notable likelihood of perinatal mortality. Conversely, a delayed diagnosis of fetal ascites was found to be connected to an elevated susceptibility to gastrointestinal disorders, particularly meconium peritonitis.

Our research recommended that further studies on the use of 4D US in the diagnosis of fetal abdominal and genito-urinary anomalies are needed on a larger sample size of pregnant women for more variety of abdominal anomalies & to confirm its efficacy in the detection of these anomalies. Further studies on different fetal body systems other than abdominal and genitourinary systems such as the central nervous system, facial, cardiac and skeletal systems are required to make sure about the diagnostic accuracy of 4D ultrasound.

5. CONCLUSIONS

4D US is a valuable adjunct to 2D US owing to its ability to improve the diagnostic capability of fetal congenital anomalies by offering additional anatomical information through its different display modes.

CONSENT

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standards written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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