The Egyptian Journal of Radiology and Nuclear Medicine 47 (2016) 1753-1764

Contents lists available at ScienceDirect



The Egyptian Journal of Radiology and Nuclear Medicine

journal homepage: www.sciencedirect.com/locate/ejrnm

Original Article



CrossMark

Mariam Raafat, Mona El-Kalioubie, Sahar Mahmoud Mansour*

Radiology Department (Women's Imaging Unit), Faculty of Medicine, Cairo University, Kasr Al-Ainy Hospital, El-Manial, 11956 Cairo, Egypt

ARTICLE INFO

Article history: Received 14 February 2016 Accepted 25 June 2016 Available online 16 July 2016

Keywords: Fetal MRI Pulmonary hypoplasia Three-dimensional ultrasound Urinary tract anomalies

ABSTRACT

Purpose: To analyze the correlation and agreement between three dimensional (3D) US and MRI in the assessment of pulmonary volumes of fetuses with different types of urinary tract malformations (UTM) and high-risk of pulmonary hypoplasia (PH).

Patients and methods: Thirty-nine fetuses with various UTM, at risk for PH were involved in this cross-sectional study. 3D volume US data sets of the fetal lungs were acquired. The right, left and total lung volumes were calculated separately using the virtual organ computer-aided analysis (VOCAL) method with a 30° rotation. MRI of fetal lung was obtained with assessment of signal intensity and lung volumetry. Comparison between mean lung volumes was performed using unpaired *t* test. Agreement between the 3D-US and MRI methods was done using Cohen kappa test.

Results: Good agreement was detected between the two methods (Kappa = 0.629, p = 0.001). The measured lung volumes by 3D-US were smaller than those measured by MRI (p > 0.05, non-significant). MRI showed greater specificity, PPV and diagnostic accuracy (100% each) than 3D-US (50%, 88.9% and 90% respectively).

Conclusion: There is a good concordance between 3D-US and MRI in the evaluation of PH in fetuses with UTM. MRI could be reserved for borderline cases of pulmonary hypoplasia and the difficult diagnostic situations.

© 2016 The Egyptian Society of Radiology and Nuclear Medicine. Production and hosting by Elsevier. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Pulmonary hypoplasia (PH) is defined as a reduction in the number of cells, airways, and alveoli in the lung that results in a decrease in the size and weight of the lung and characteristically causes severe respiratory failure that leads to neonatal death [1].

One of the main causes of PH is oligohydramnios due to prolonged rupture of membranes and urinary tract malformations (UTMs) [2]. A fatal outcome is commonest with bilateral renal agenesis and bladder outlet obstruction, but also occurs with bilateral renal dysplasia/hypoplasia and multicystic kidney [3].

The data suggest that the kidneys are important in early lung growth, while the presence of amniotic fluid contributes to growth later in gestation. Many studies have shown poor outcome and low survival in fetuses with

http://dx.doi.org/10.1016/j.ejrnm.2016.06.014

Peer review under responsibility of The Egyptian Society of Radiology and Nuclear Medicine.

^{*} Corresponding author.

E-mail addresses: mariam_raafat@yahoo.com (M. Raafat), monaelkalioubie@yahoo.com (M. El-Kalioubie), sahar_mnsr@yahoo.com (S.M. Mansour).

⁰³⁷⁸⁻⁶⁰³X/© 2016 The Egyptian Society of Radiology and Nuclear Medicine. Production and hosting by Elsevier. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

oligohydramnios, especially when prolonged, developing before 26–28 weeks of gestation [4].

Accurate antenatal and neonatal diagnosis of PH provides an option for parents counseling and probability of pregnancy termination [5].

However prenatal diagnosis of PH is a major clinical challenge [6,7]. Since it is due to reduction in size and weight of the lungs, the volumetric lung evaluation seems to be an accurate form of predicting this condition [8]. Three-dimensional 3D-US provides a simple and inexpensive tool for lung volume calculation, in addition to rotational measurements of volume which is possible through the introduction of a software tool called Virtual Organ Computer-aided Analysis (VOCAL) [9].

While this technique allows access to all possible views and accurate determination of organ volume, it may be affected by fluid volume or maternal obesity and fetal position [10].

Several studies in the last years have demonstrated that it is possible to estimate the fetal lung volume in utero through magnetic resonance imaging (MRI) [11–13]. Fetal MRI offers operator-independent imaging in a number of different planes, with excellent soft tissue contrast and a large field of view. Furthermore, it is less affected by maternal habitus, fetal position, or low levels of amniotic fluid [14,15].

The aim of this work was to evaluate the concordance between 3D-US and MRI in the assessment of lung volume in fetuses with urinary tract malformations. Furthermore we wanted to investigate whether the two methods can be used interchangeably in fetuses at high risk of PH. Conditions in which it would be useful to use MRI as an adjunct or complementary method to US were highlighted.

2. Patients and methods

2.1. Patients

Various fetal urinary tract anomalies were evaluated in 39 singleton pregnancies between January 2013 and January 2015. The institutional review board approved this cross-sectional study.

Patients were recruited during their regular antenatal care referred from the Gynecology and Obstetrics department after performing their routine antenatal 2D-US. Gestational age was established by menstrual dates and confirmed by routine fetal biometry (biparietal diameter, head circumference, abdominal circumference, femoral diaphysis length), as well as transverse cerebellar diameter.

Inclusion criteria were single living fetus with a gestational age ranging from 20 to 36 weeks by conventional menstrual dating (last menstrual period). Amniotic fluid index (AFI), fetal position and detailed fetal anatomy were assessed. On the basis of the patient's medical history, clinical status and the sonographic findings of unilateral or bilateral urinary tract malformations that are commonly detected (e.g. bilateral infantile polycystic kidney disease, multicystic dysplastic kidney/s, renal agenesis and posterior urethral valve), associated with an oligohydramnios, included fetuses were those at high risk for pulmonary hypoplasia.

We excluded twin pregnancies, fetuses with skeletal anomalies associated with narrow chest or congenital abnormalities affecting the lungs. We also excluded pregnant women non-eligible for MRI examination (due to claustrophobia or presence of pace makers).

Patients ranged in age from 18 to 35 years with a mean of 25.8 years \pm 4.53 (mean \pm SD).

2.2. Imaging protocol

*US examination was performed using Voluson 730D 3D-US system (kretztechnik AG, Zipf, Austria). A transabdominal convex array volume transducer with frequency range 3.0–5.0 MHz was employed for 2D-US and to acquire the 3D volume data set.

The following parameters were assessed in each fetus:

- Fetal biometry, position, viability and biophysical profile.
- The amount of amniotic fluid was calculated using four quadrants amniotic fluid index, the reference values proposed by Moore and Cayle [16].
- Lung assessment by 2D-US including lung echogenicity.
- 3D-US volumetry using VOCAL technique. Harmonic imaging was used to obtain a better contrast between the lungs and abdominal organs. The slowest scan duration was adjusted to obtain the best resolution. Intersection of the 4 cardiac chambers was used as the reference plane for volumetric lung assessment. A sweep angle of 40–85° was used, depending on gestational age at the time of the test. A sequence of six sections of each lung around a fixed axis was obtained, from the apex to the base, each after a 30° rotation from the previous section. A transverse section of the fetal thorax was chosen and each volume was measured using the rotational technique, outlining the contour of the lung 6 times. Right and left lung volumes were obtained for each fetus. Total fetal lung volume was calculated by adding the mean volume of both lungs. The calculated lung volumes were compared to established nomograms published by Ruano et al. [17].
- Color Doppler was selected to assess vascularity in selected cases.
 - MRI examination was done within one week from the US examination. The patients were instructed to fast 4 h prior to the examination to reduce bowel peristalsis artifacts, to prevent postprandial fetal motion and to empty their bladder immediately before undergoing MRI. Sedation was not needed.

MR imaging was performed with 2 MRI machines: A 1.5-T magnet (Vision; Philips Gyroscan Intera and Achieva); both equipped with a phased-array pelvic coil. Patients lied in the supine position. After a scout acquisition, a series of fetal images in the axial, sagittal, and coronal planes were obtained including the following:

- T2 weighted images using a single-shot rapid acquisition and relaxation enhancement sequence, with a repetition time of 100-140 ms, an effective echo time of 90 ms, and a matrix of $256 \times 160-256$. Section thickness and intersection gap were 4–6 and 0 mm respectively and 30–35 cm field of view (FOV).
- Fast gradient-echo sequence, (balanced FFE) with TR/TE of 3.5/1.8, flip angle 60° and single shot turbo spin echo sequences with TR/TE of 1000/80 and matrix of 200×240 , slice thickness and intersection gap of 4–6 mm and 0 respectively and 30–35 cm FOV.

MRI examination took from 10 to 20 min and was well tolerated by all patients. Image quality was diagnostically satisfactory in all patients, and fetal movements did not alter image quality, although no maternal sedation was used. Lung volume was calculated by selecting the single-shot sequence that allowed complete imaging of both lungs without motion or section misregistration artifact. The cross-sectional area of each lung section was measured on a workstation (Philips View Forum 7.2.0.1) by free form region of interest (ROI) tool. The area was multiplied by section thickness and intersection gap to determine the volume for that section (N.B: we used 0 intersection gap so it was omitted from the calculation). The volumes for all sections were then added to determine the volume of the entire lung. The calculation was repeated for the contralateral lung, and the volumes of both lungs were combined to determine the total lung volume. The calculated lung volumes were compared to established nomograms as published by Cannie et al. [18].

Lung signal intensity on T2WIs was also used to assess lung maturity through comparing it to the amniotic fluid, and surrounding muscles. It was considered normal if similar to or slightly less than the amniotic fluid signal (according to gestational age) and abnormal when approaching surrounding muscle signal.

For pregnancies completed to term, diagnosis of pulmonary hypoplasia was ascertained by clinical and radiological criteria that were our reference standard.

Clinical criteria were categorized as follows: good postnatal respiratory outcome with no respiratory distress that did not require endotracheal intubation and mechanical ventilation, or poor respiratory outcome, with the immediate onset of severe respiratory insufficiency after birth, small lung capacity, resulting in neonatal death or a requirement for high ventilatory pressure in the absence of an obstruction or atelectasis.

Radiological criteria were defined via post-natal imaging using US for diagnosis of renal anomalies. In case associated CNS anomalies (e.g. Meckel–Gruber syndrome) were suspected MRI was done and chest X-ray was done for confirmation of pulmonary hypoplasia in surviving fetuses. Imaging features of perinatal lethal pulmonary hypoplasia included small lung fields with diaphragmatic domes raised up to the 7th rib, downward-sloping, a bell-shaped chest, and/or pneumothorax or pneumomediastinum.

There were 9 terminated pregnancies (beyond 24 weeks) due to lethal anomalies.

2.3. Statistical analysis

Statistical Package for the Social Science (SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows computer program was used for data analysis. Maternal age and gestational ages were presented as means, standard deviation (SD), minimum and maximum values. Comparison between lung volume variables in the two groups was performed using unpaired *t* test. Agreement between the US and MRI techniques was done using kappa test. *Z* score was then calculated to test statistical significance. *P* values less or equal to 0.05 were considered significant and less than 0.01 highly significant. Standard diagnostic indices including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy were calculated for 3D-US and for MRI.

3. Results

Fetuses included in the study presented with a gestational age ranging from 20 to 36 weeks by conventional menstrual dating (last menstrual period) (mean 28.8 weeks \pm 4.24) and from 21 to 34 by average US date (mean 28.5 \pm 3.99).

The studied group presented with various UTM ranging from cases with good prognosis to lethal ones, such as bilateral renal agenesis (Fig. 1).

3.1. Neonatal outcome

Pregnancy was terminated (beyond 24 weeks) in 9 (23.1%) cases due to lethal anomalies, 15 (38.5%) died shortly after birth due to severe respiratory distress, 9 (23.1%) cases required mechanical ventilation and 6 (15.3%) had good respiratory outcome.

3.2. Lung volume

The total lung volume as measured by 3D-US and MRI in different gestational ages of the studied population is shown in Fig. 2.

Hypoplastic lungs were hypoechoic on 3D-US and elicited low T2 signal intensity on MRI approaching the surrounding muscles signal (Fig. 3).

The measured lung volumes by 3D-US were smaller than those measured by MRI however with non-significant p value (p > 0.05).

Table 1 and Fig. 4 demonstrate the different mean values of right, left and total lung volumes as measured by 3D-US and MRI in the studied population.

3.3. Agreement between 3D-US and MRI

US suggested PH in 36 (93.3%) out of the 39 studied fetuses, while MRI suggested 33 (84.6%) cases with PH. US and MRI disagreed on 3 cases: in those 3 (7.7%) cases, MRI provided accurate estimation of normal lung volume (true negative) while US diagnosed bilateral PH (false positive) (Fig. 5). The agreement between 3D-US and MRI, as regards a diagnosis of PH was obtained in 33 out of the





Fig. 1. Twenty-six-week fetus with bilateral renal agenesis, situs inversus total and pulmonary hypoplasia. (a) Color Doppler 2D-US shows absent kidneys. (b) 3D-US measuring right and left lung volumes using VOCAL technique, displays hypoplastic lungs with total volume = 6.98 ml (normal for age = 23–37 ml). (c) Coronal MRI single shot FSE T2 images of fetal chest and upper abdomen show reduced signal intensity of both lungs approaching that of surrounding muscles. The total lung volume is 15 ml (normal for age = 23.6–37.5 ml). (d) Axial MRI T2 images of the fetal abdomen show absent kidneys. The newborn died shortly after birth.

1756

M. Raafat et al. / The Egyptian Journal of Radiology and Nuclear Medicine 47 (2016) 1753-1764



Fig. 1 (continued)



Fig. 2. Diagram presenting the correlation between total lung volume and gestational age measured by MRI and 3D-US in the studied population.

39 studied fetuses. Finally 3 (7.7%) cases with unilateral multicystic dysplastic kidney showed normal lung volume on both US and MRI.

The strength of agreement between the two methods in establishing a diagnosis of PH was considered to be good (substantial) (Kappa = 0.629, 95% Confidence Interval ranged from 0.254 to 1.000). The standard error of Kappa was SE = 0.191. *Z* score to test the statistical significance of kappa was 3.293. *P* value was 0.0010 which is therefore extremely statistically significant.

3.4. Neonatal outcome agreement with 3D-US and MRI respectively regarding PH

- 3D-US, MRI and post-natal outcome (clinical examination/post-natal US) agreed on 24 (61.5%) cases to have PH.
- There were 3 (7.7%) cases of disagreement between neonatal outcome and 3D-US, two cases of bilateral infantile polycystic kidneys and one case that presented with bilateral hydronephrosis and hydroureter as well as distended urinary bladder (diagnosed with posterior urethral valve (PUV)). All showed bilateral lung hypoplasia by US and normal post-natal respiratory outcome with no clinical evidence of PH. They also had normal lung volume by MRI.
- There was agreement between 3D-US, MRI and postnatal outcome in another 3 (7.7%) cases of unilateral multicystic dysplastic kidney that presented with normal lung volumes.
- In nine (23.1%) cases, agreement between prenatal radiology and post-natal outcome could not be evaluated due to termination of pregnancy. Final evaluation was based on radiological and clinical criteria of lung maturity.

M. Raafat et al./The Egyptian Journal of Radiology and Nuclear Medicine 47 (2016) 1753-1764



Fig. 3. Thirty-week fetus with bilateral multicystic dysplastic kidneys and pulmonary hypoplasia. (a) 3D-US measuring right lung volume (6.9 ml) and (b) 3D-US measuring left lung volume (5.6 ml) using VOCAL technique, display hypoplastic lungs with total volume = 12.5 ml (normal for age = 40–64 ml). (c) Coronal MRI single shot FSE T2 images of fetal chest and upper abdomen show reduced signal intensity of both lungs approaching that of surrounding muscles. The total lung volume is 16.9 ml (normal for age = 45 ml). Bilateral enlarged kidneys with bright signal and multiple variable sized cysts are seen. Severe respiratory distress led to death shortly after birth.

Table 1

Comparison between mean values of right, left and total lung volumes measured by 3D-US and MRI. Data are expressed as mean \pm SD. NS = p > 0.05 = non-significant.

	Right lung volume	Left lung volume	Total lung volume
3D-US MRI Mean difference	11.3 ± 9.5 12.95 ± 10.7 1.65	9.38 ± 7.5 11.89 ± 9.1 2.51	20.68 ± 17 24.99 ± 19.6 4.31
p Value	0.47 (NS)	0.19 (NS)	0.30 (NS)

Based on our reference standards, MRI predicted the correct diagnosis and showed normal lung volumes in 3 cases that were wrongly diagnosed as PH by 3D-US (3 false positive).

Relying on the previous findings, the diagnostic indices of 3D-US and MRI regarding the diagnosis of PH are calculated (we used only the 30 cases that completed pregnancy, to assess fetal respiratory outcome). MRI showed greater specificity, PPV and diagnostic accuracy (100% each) than 3D-US (50%, 88.9% and 90% respectively) in



Fig. 4. Bar chart showing comparison between mean value of right, left and total lung volume measured by US and MRI.



Fig. 5. Thirty-two-week fetus with bilateral infantile polycystic kidneys. (a) 2D-US shows bilateral large echogenic kidneys (arrows). (b) 3D-US that shows measurements of the right lung volume and (c) 3D-US measuring left lung volume using VOCAL technique, displays hypoplastic lungs with total volume = 38.94 ml (normal for age = 49-76 ml). (c) Coronal MRI single shot FSE T2 images of fetal chest and upper abdomen show large hyperintense kidneys. Lungs show total volume = 73.5 ml (normal for age = 60-75 ml) and normal T2 signal intensity as well. Normal respiratory outcome at birth, no pulmonary hypoplasia but the infant died at 6 months due to renal failure.

M. Raafat et al./The Egyptian Journal of Radiology and Nuclear Medicine 47 (2016) 1753-1764



Fig. 5 (continued)

the diagnosis of pulmonary hypoplasia in the studied group. They had similar sensitivity and NPV (100% each).

3.5. Agreement between 3D-US and MRI in diagnosing urinary tract anomalies

Both 3D-US and MRI diagnosed similar urinary tract anomalies in 35 (89.7%) out of 39 patients. MRI added extra-urinary finding of occipital encephalocele in one case (Fig. 6) and changed the diagnosis in 3 cases (Table 2).

There was an appreciable association between urinary tract abnormalities and PH, as among 39 cases suffering from UTM, 33 (84.6%) had associated PH and 6 (15.4%) had normal lung volumes on MRI volumetry (Fig. 5). The studied group presented with various UTM ranging from cases with good prognosis to lethal ones, such as bilateral renal agenesis.

Table 3 shows the association between urinary tract anomalies and PH by MRI in the studied group.

4. Discussion

Antenatal prediction of the severity of lung hypoplasia remains a challenging issue in maternal-fetal medicine. Infants with pulmonary hypoplasia (PH) require intensive monitoring and care immediately after birth. Accurate prenatal quantification of PH can help in the choice of management options, including termination of pregnancy, planned delivery with intensive monitoring, post-natal therapy, and fetal surgery [19].

This study included 39 fetuses with various types of UTM, ranging from cases with good prognosis to lethal ones, such as bilateral renal agenesis. All cases presented with either anhydramnios or oligohydramnios. Thirty-three (84.6%) cases had associated PH and only six cases (15.4%) had normal lung volumes. This is comparable with the literature findings. In the study conducted by Junior et al., five fetuses with urinary malformations had developed pulmonary hypoplasia, four of them had severe oligohydramnios (AFI = 0) and one case had normal AFI [2]. On the other hand seven fetuses, also with urinary anomalies had normal lung volumes as well as normal amniotic fluid volume. In a study conducted by Rezende et al., most of the fetuses with lethal pulmonary hypoplasia (18/47) were affected by renal and UTM [7].

3D-US has been described as the screening imaging modality of choice that can provide accurate visualization of the anatomy of the fetus and uterus. Yet, optimal 3D-

M. Raafat et al./The Egyptian Journal of Radiology and Nuclear Medicine 47 (2016) 1753-1764



Fig. 6. Twenty-eight-week fetus with Meckel–Gruber syndrome and pulmonary hypoplasia. (a) 2D-US shows bilateral large echogenic kidneys diagnostic of bilateral infantile polycystic kidneys. (b) 2D-US shows a large posterior fossa cyst (Dandy-Walker malformation). (c) 3D-US measuring right lung volume and (c) 3D-US measuring left lung volume using VOCAL technique, display hypoplastic lungs with total volume = 21.64 ml (normal for age = 31–50 ml). (c) Coronal single shot MRI FSE T2 images of fetal brain, chest and upper addomen show large posterior fossa cyst communicating with the 4th ventricle, large hyperintense kidneys. The lungs depict a lower than normal signal close to that of surrounding muscles. Total lung volume is 24.5 ml (normal for age 36.5–56.1 ml) diagnostic of pulmonary hypoplasia. (f) Sagittal MRI single shot FSE T2 image of the fetus shows an occipital encephalocele. Termination was done at 29 weeks.

US resolution may not always be possible owing to fetal position, oligohydramnios, maternal obesity, fetal cardiac activity and fetal breathing movements. The accurate delineation of the contour of the lung may be hampered because of reduced differentiation between fetal lung and liver [20].

Recently, MRI can be used to evaluate lung development. Such evaluation includes assessment of signal intensity, volumetric measurements, echoplanar imaging, and MR spectroscopy [21].

In this study, we assessed the concordance between 3D-US and MRI in the assessment of pulmonary volumes of fetuses with different types of urinary tract anomalies with associated oligohydramnios and are at risk for PH. We chose to study this group since previous literatures considered brain pathology and only a small number of researchers studied the use of MRI in the assessment of genitourinary abnormalities.

In our study we used the VOCAL3D-US method with a 30° rotation angle. Previous studies have demonstrated

that this method is more accurate than the multiplanar method in the evaluation of irregularly shaped objects [22].

Lung volume assessment in fetuses presented with oligohydramnios is crucial, since there is associate considerable degree of pulmonary architecture distortion. Right, left and total lung volumes using 3D-US and MRI were measured in all of our cases. Similarly, in a recent study, Junior et al. were able to measure all lung volumes using 3D-US and MRI in 12 patients with UTM [2].

In a study performed by Cannie et al., the mean total fetal lung volume measured by MRI in 36 fetuses with normal lungs was 58.29 ml. Total fetal lung volume ranged from 10.16 ml at 18 weeks to 132.05 ml at 39 weeks [14]. In our study the mean total fetal lung volume measured by MRI in 6 fetuses with no evidence of pulmonary hypoplasia was 64.53, with total lung volumes ranging from 49.3 ml at 23 weeks gestation to 67.4 ml at 35 weeks gestation.

M. Raafat et al./The Egyptian Journal of Radiology and Nuclear Medicine 47 (2016) 1753-1764



Fig. 6 (continued)

Table 2	
Types of disagreement between US and MRI.	

US findings	MRI findings	
Bilateral infantile polycystic kidneys + Posterior fossa cyst (Dandy-Walker malformation)	MRI added finding of occipital encephalocele	
Right hydronephrosis and hydroureter	Bilateral small multicystic dysplastic kidneys with small non communicating cysts	
Non-visualized left kidney	Cerebellar hypoplasia diagnosing Meckel–Gruber syndrome	
Large pelvi-abdominal cyst	Obstructive uropathy, megacystis with multiple diverticula likely due to posterior urethral valve Small dysplastic kidneys	
Bilateral hydronephrosis and hydroureter (vesico-ureteric obstruction)	Bilateral hydronephrosis with dilated extrarenal pelvis No ureteric dilatation changing diagnosis to pelviureteric junction obstruction instead of vesicoureteric obstruction	

Ruano et al. obtained a total of 146 normal lung volumes by 3D-US where the right mean lung volume ranged from 5.37 ml at 20 weeks to 46.06 ml at 37 weeks. The left mean lung volume ranged from 4.66 ml at 20 weeks to 37.34 ml at 37 weeks. The total mean lung volume ranged

Table 3

Association between urinary tract abnormalities and lung hypoplasia by MRI in the studied group.

	Lung hypoplasia by MRI	
	No	Yes
Positive urinary tract anomalies $(n = 39)$	6 (15.4%)	33 (84.6%)

from 9.95 ml at 20 weeks to 84.35 ml at 37 weeks [17]. In our study, US detected normal lung volumes in 3 cases where the mean total lung volume was 62.5 ml at 35 weeks gestation.

Daltro et al. stated that lungs typically contain a significant amount of alveolar fluid, which is homogeneously hyperintense relative to the chest wall muscle on T2weighted images. In cases of lung compression, the amount of alveolar fluid is decreased, resulting in a more hypointense signal [23]. We agreed with this as we found all cases with pulmonary hypoplasia to show significantly hypointense T2 signal approaching the muscles signal while normal lungs elicited bright T2 signal like or slightly less than the surrounding amniotic fluid. This is similarly applied to the lung echogenicity in 3D-US, where hypoplastic lungs were much more hypoechoic than normal lungs, conforming to findings of Schwach et al. [24].

Gerards et al. compared between the lung volume measurements by MRI and 3D-US performed in uncomplicated pregnancies. They showed high interclass correlations and small mean differences, where the mean difference between right lung volumes as measured by 3D-US and MRI was 2.13 and that of the left lung was 0.86 (non-significant) [25].

In our study, the mean difference of the right lung volume as measured by 3D-US and MRI was 1.65 ml (p value = 0.47, non-significant), that of the left lung was 2.51 ml (p value = 0.19, non-significant) and that of the total lung volume was 4.31 ml (p value = 0.41, non-significant).

Peralta et al. [9] observed that 3D-US underestimated the fetal lung volumes when compared with MRI, and we agreed with this observation where all measured lung volumes were smaller by 3D-US than by MRI; however, this did not alter the diagnosis except in 3 out of 39 cases representing 7.7% (false positive cases). Junior et al. obtained similar results, where on comparing the mean values, both 2D-US and 3D-US tended to underestimate the volumes when compared to MRI [2].

Several reports in the literature have shown good agreement between 3D-US and MRI in the estimation of fetal lung volumes. Ruano et al. compared lung volume measurements with 3D-US VOCAL technique and MRI in 11 cases of congenital diaphragmatic hernia and a good agreement; intraclass correlation (ICC = 0.94) was achieved [26]. Junior et al. [2] showed a good concordance between 3D-US and MRI in the evaluation of lung volume in fetuses with urinary tract anomalies. There was a strong correlation between lung volumes assessed through MRI, 2D-US and 3D-US (done with VOCAL technique at different rotation angles 30, 18 and 12), for both the right and left lungs. For the right lung, the ICC was 0.909; 0.913; 0.883 for MRI vs. VOL30; MRI vs. VOL18 and MRI vs. VOL12 respectively. As for the left lung they were 0.924; 0.947; and 0.940 respectively. In our study we also showed good agreement between the two techniques proved by Cohen Kappa, which was 0.629 (p = 0.0010, extremely statistically significant).

Cannie et al. stated that superior tissue contrast, a large field of view and relative operator independence enable fetal MRI to provide information that can supplement the information obtained by prenatal US examination, and concluded that MRI is more reliable than 2D or 3D-US for assessing the degree of PH mainly in cases of CDH [18]. In our study, MRI added to the prenatal US diagnosis of fetal anomalies in one case and changed the diagnosis in three cases. Also it showed greater agreement with neonatal outcome: 3D-US, MRI and post-natal outcome (clinical examination/post-natal X-ray/postnatal US) agreed on 24 (61.5%) cases to have pulmonary hypoplasia. There were 3 (7.7%) cases of disagreement between neonatal outcome and 3D-US: two cases of bilateral infantile polycystic kidneys and one case with PUV. All showed bilateral lung hypoplasia by US and normal post-natal respiratory outcome. They also had normal lung volume by MRI. Therefore, based on our reference standards, MRI managed to correct the diagnosis and show normal lung volumes in three cases that were wrongly diagnosed as PH by 3D-US (3 false positive).

Junior et al. stated that 3D-US was 100% accurate in the assessment of lung volumes of fetuses with various types

of UTM, with normal and reduced amniotic fluid [2]. In our study MRI showed greater specificity, PPV and diagnostic accuracy (100% each) than 3D-US (50%, 88.9% and 90% respectively) in the diagnosis of PH in the studied group. They had similar sensitivity and NPV (100% each).

Our study had some limitations: There was no clear cutoff between lethal and non lethal PH which needs further studies on larger samples. Also the VOCAL technique was done only with a 30° rotation angle and did not make use of other possible rotation angles.

5. Conclusion

There is good agreement between 3D-US and MRI in the assessment of lung volume in fetuses with urinary tract malformation. MRI proved to be more specific and accurate in diagnosing PH and the associated fetal anomalies, thus may be used complementary to US especially in (i) inconclusive cases and (ii) prior elective pregnancy termination to confirm lung maturity.

Conflict of interest

The authors declare no conflict of interests.

References

- [1] Tanigaki S, Miyakoshi K, Tanaka M, Hattori Y, Matsumoto T, Ueno K, et al. Pulmonary hypoplasia: prediction with use of ratio of MR imaging-measured fetal lung volume to US-estimated fetal body weight. Radiology 2004;232(3):767–72.
- [2] Junior EA, De Oliveira PS, Nardozza LMM, Simioni C, Rolo LC, Goldman SM, et al. Fetal lung volume in fetuses with urinary tract malformations: comparison by 2D-, 3D-sonography and magnetic resonance imaging. J Maternal-Fetal Neonatal Med 2010;23(1):60–8.
- [3] Greenough A, Blott M, Nicolaides K, Campbell S. Interpretation of fetal breathing movements in oligohydramnios due to membrane rupture. Lancet 1988;1:182–3.
- [4] Rubesova Erika. Why do we need more data on MR volumetric measurements of the fetal lung? Pediatr Radiol 2016;46:167-71
- [5] May C, Greenough A. Pulmonary hypoplasia and congenital renal anomalies. Arch Med Sci 2006;2(1):6–9.
- [6] Kalache KD, Espinoza J, Chaiworapongsa T, Londono J, Schoen ML, Treadwell MC, et al. Three-dimensional ultrasound fetal lung volume measurement: a systematic study comparing the multiplanar method with the rotational (VOCAL) technique. Ultrasound Obstet Gynecol 2003;21:111–8.
- [7] Rezende GC, Pereira AK, Júnior EA, Reis ZSN, Cabral ACV. Prediction of lethal pulmonary hypoplasia among high-risk fetuses via 2D and 3D ultrasonography. Int J Gynecol Obstetrics 2013;123:42–5.
- [8] Chang CH, Yu CH, Chang FM, Ko HC, Chen HY. Volumetric assessment of normal fetal lungs using three-dimensional ultrasound. Ultrasound Med Biol 2003;29:935–42.
- [9] Peralta CF, Cavoretto P, Csapo B, Falcon O, Nicolaides KH. Lung and heart volumes by three-dimensional ultrasound in normal fetuses at 12–32 weeks' gestation. Ultrasound Obstet Gynecol 2006;27 (2):128–33.
- [10] Ruano R, Marie-Cecile A, Dumez Y, Zugaib M, Alexandra B. Predicting neonatal deaths and pulmonary hypoplasia in isolated congenital diaphragmatic hernia using the sonographic fetal lung volume-body weight ratio. AJR 2008;190:1216–9.
- [11] Rypens F, Metens T, Rocourt N, Sonigo P, Brunelle F, Quere MP, et al. Fetal lung volume: estimation at MR imaging – initial results. Radiology 2001;219:236–41.
- [12] Osada H, Kaku K, Masuda K, Iitsuka Y, Seki K, Sekiya S. Quantitative and qualitative evaluations of fetal lung with MR imaging. Radiology 2004;231:887–92.
- [13] Ward VL, Nishino M, Hatabu H, Estroff JA, Barnewolt CE, Feldman HA, et al. Fetal lung volume measurements: determination with MR imaging – effect of various factors. Radiology 2006;240:187–93.

- [14] Cannie M, Jani J, De Keyzer F, Devlieger R, Van Schoubroeck D, Witters I, et al. Fetal body volume: use at MR imaging to quantify relative lung volume in fetuses suspected of having pulmonary hypoplasia. Radiology 2006;241:847–53.
- [15] Cannie M, Jani J, Dymarkowski S, Deprest J. Fetal magnetic resonance imaging: luxury or necessity? Ultrasound Obstet Gynecol 2006;27:471–6.
- [16] Moore TR, Cayle JE. The amniotic fluid index in normal human pregnancy. Am J Obstet Gynecol 1990;162:1168–73.
- [17] Ruano R, Joubin L, Aubry M, Thalabard Dommergues M, Dumez Y, et al. Nomogram of fetal lung volumes estimated by 3-dimensional ultrasonography using the rotational technique (virtual organ computer-aided analysis). J Ultrasound Med 2006;25:701–9.
- [18] Cannie M, Jani J, Van Kerkhove F, Meerschaert J, De Keyzer F, Lewi L, et al. Fetal body volume at MR imaging to quantify total fetal lung volume: normal ranges. Radiology 2008;247:197-203.
- [19] Bunduki V, Ruano R, Silva M, Miguelez J, Miyadahira S, Maksoud JG, et al. Prognostic factors associated with congenital cystic adenomatoid malformation of the lung. Prenat Diagn 2000;20:459–64.
- [20] Gerards FA, Engels MA, Twisk JW, van Vugt JM. Normal fetal lung volume measured with three-dimensional ultrasound. Ultrasound Obstet Gynecol 2006;27(2):134–44.

- [21] Brown S, Estroff J, Barnewolt C. Fetal MRI in the evaluation of chest anomalies: a pictorial essay. Appl Radiol 2004;33(2):215–30.
- [22] Jani JC, Cannie M, Peralta CF, Deprest JA, Nicolaides KH, Dymarkowski S. Lung volumes in fetuses with congenital diaphragmatic hernia: comparison of 3D US and MR imaging assessments. Radiology 2007;244:575–82.
- [23] Daltro P, Werner H, Gasparetto T, Domingues R, Rodrigues P, Marchiori E, et al. Congenital chest malformations: a multimodality approach with emphasis on fetal mr imaging. RadioGraphics 2010;30:385–95.
- [24] Schwach I, Britto W, Cláudio L, Bussamra D, Júnior E, Drahem G, et al. Fetal lung volume: comparison by 2D- and 3D-sonography in normal fetuses. Arch Gynecol Obstet 2009;280:363–8.
- [25] GerardS F, Twisk J, Bakker M, Barkhof F, Van Vugt J. Fetal lung volume: three-dimensional ultrasonography compared with magnetic resonance imaging. Ultrasound Obstet Gynecol 2007;29:533–6.
- [26] Ruano R, Joubin L, Sonigo P, Benachi A, Thalabard J, Brunellew F, et al. Fetal lung volume estimated by 3-dimensional ultrasonography and magnetic resonance imaging in cases with isolated congenital diaphragmatic hernia. J Ultrasound Med 2004;23:353–8.