Original Article

In utero MRI diagnosis of fetal malformations in oligohydramnios pregnancies

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A B S T R A C T

Objective: To evaluate the role of MRI in assessing Ultrasonographically (US)-suspected fetal malformations associated with oligohydramnios.

Methods: We performed MRI in 43 oligohydramnios pregnancies referred with US-suspected fetal malformations at a mean of 25.5 weeks’ gestation. MRI findings were correlated with US data and outcome measures.

Results: MRI correctly diagnosed one normal fetus suspected to have posterior cephalocele. In the remaining 42 fetuses who had malformations involving their urinary systems (n = 36), brains (n = 23), bones (n = 4), hearts (n = 3), and hepatobiliary (n = 3), MRI confirmed US diagnosis in 25 fetuses (58.1%), and added US-occult findings in 14 (32.5%) that were mainly related to the brain, urinary and hepatobiliary system. In 2 fetuses (4.7%), MRI added findings but missed data correctly detected by US in another 2 fetuses. MRI missed fetal skeletal and cardiac function abnormalities correctly detected by US. MRI accurately detected multiple body system abnormalities that aided prenatal correct diagnosis of syndromes including Meckel Gruber (n = 15) and Joubert syndrome and related cerebellar disorders (n = 1).

Conclusion: MRI is valuable in evaluating suspected fetal malformations especially those related to brain and urinary system when ultrasound is inconclusive owing to oligohydramnios. Fetal MRI can add findings that may modify prenatal diagnosis.

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Abbreviations: Abd, abdominal; ACC, agenesis of corpus callosum; ARPKD, autosomal recessive polycystic kidney; bilat, bilateral; BV, born viable; CH, cerebellar hypoplasia; CMV, cytomegalovirus; CT, computed tomography; DWM, Dandy-Walker malformation; GA, gestational age; JSRD, Joubert syndrome and related cerebellar disorders; L, left; LH, left heart; MCDK, multi-cystic dysplastic kidney; MKS, Meckel Gruber syndrome; MMH, megacystis microcolon hypoperistalsis; MRI, magnetic resonance imaging; MRU, magnetic resonance urography; MTS, molar tooth sign; Obst, obstruction; PC, posterior cephalocele; PM, post-mortem; Post, posterior; PUJ, pelvi-ureteric junction; PUV, posterior urethral valve; RH, right heart; SA, spontaneous abortion; TA, therapeutic abortion; UB, urinary bladder; Unilat, unilateral; US, ultrasonography; UV, uretero-vesical; VCUG, voiding cysto-urethrogram; VM, ventriculomegaly; VSD, ventricular septal defect.

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1. Introduction

The amniotic fluid that surrounds the fetus is necessary for its proper development. Fetal urine is the main source of amniotic fluid in the last two-thirds of pregnancy [1]. Pregnancies associated with inadequacy of amniotic fluid volume (oligohydramnios), are often associated with congenital anomalies, both deformations and malformations [2]. Deformation is the process of disfiguring a pre-existing part of the body, while malformation is the process of disrupting the original stages of organ development [3]. In oligohydramnios sequence, the decrease in fluid causes intrauterine mechanical constraints that result in fetal deformations of flat facial profile (Potter’s facies), limb deformities, chest compression and pulmonary hypoplasia [1], while fetal malformations associated with oligohydramnios are mainly urinary, musculoskeletal, digestive and cardiac in nature [2]. Oligohydramnios has a high perinatal mortality rate and requires careful fetal examination [4].

Although ultrasonography (US) remains the primary imaging technique for evaluating the developing fetus, oligohydramnios implies significant limitations to US assessment of fetal anatomy and suspected malformations [1,5]. MR imaging does not suffer from oligohydramnios restraints and has proved to be a useful prenatal imaging modality of fetal abnormalities [6,7].

The aim of this study was to assess the role of MRI in assessing ultrasonographically suspected fetal malformations associated with oligohydramnios.

2. Materials and methods

We performed MRI for 43 consecutive oligohydramnios singleton pregnancies referred with US-suspected fetal malformations, in this institutional-approved study. The mean maternal age was 25 years (SD 5.2, range 18–40). The mothers gave no history of ruptured membranes, hypertension, diabetes mellitus, or intake of medications during the current pregnancy. Twenty-one pregnancies were the result of consanguineous marriages. Thirteen patients gave past history of 19 pregnancies with anomalous fetuses that included autosomal recessive polycystic kidney disease (ARPKD) (n = 7), Meckel Gruber syndrome (MKS) (n = 9), anencephaly (n = 1), and posterior cephalocele (PC) (n = 2) (see Figs. 1 and 2).

All examined pregnancies were singleton at an average of 25.5 weeks of gestation (SD 6) (range 17–39). The gestational age (GA) was based on the last menstrual period and/or the earliest US biometric measurements done during the pregnancy (see Figs. 3–5).

All pregnancies referred to MRI showed significant oligohydramnios (Amniotic Fluid Index was less than 5 cm) and were associated with suspected fetal malformation according to detailed prenatal 2D- and 3D-US studies. Only primary fetal malformations were included in our study. Fetal deformations, such as pulmonary hypoplasia and skeletal deformities that result from prolonged oligohydramnios were not studied.

US examination was performed at specialized obstetric US imaging unit at our institution using 3.5–5 MHZ 3D transducer (Voluson 730 ProV, GE Healthcare, Milwaukee, WI, USA). An obstetric record was provided for each patient including fetal measurements, amount of amniotic fluid, and complete assessment for fetal anomalies. The static and real-time digital images of all of the US studies were archived.

Fetal MRI was performed in the same day or within 3 days of the US examination (average 1.09 SD 1.1 days) using 1.5 T superconducting systems (Intera, Philips Medical Systems, Best, Netherlands or Gyroscan Achieva, Philips Medical Systems, Best, Netherlands) using a phased-array...
No patients were excluded because of contraindication to MRI or claustrophobia. Most patients were positioned supine and head first into the gantry. Patients who could not lie supine were put in the left lateral decubitus. MR imaging was obtained along fetal body planes using T2-weighted single shot fast spin echo (SSh) (TTR/TE 10,000/100 ms, 4-mm slice thickness, matrix 196 x 256 or 256 x 256) and steady state free precession sequence (TR/TE 3.5–4 ms/1.7–2 ms, FA 60–90, 1–2 signals acquired, 256 x 256 matrix, and 4 mm slice thickness with no inter-slice gap). Additional T1-weighted MR images were obtained using a breath-hold spoiled gradient echo sequence (100–140/4.2) (repetition time TR msec/echo time TE msec), 70–90° flip angle (FA), 256 x 160–256 matrix, one signal acquired, slice thickness between 4 and 6 mm with an inter-slice gap of 0.2–0.4 mm. No contrast agent, sedative, or fetal paralysis were used. All fetal MRI examinations and MR images in this study were approved at the time of acquisition by attending radiologist experienced in MRI and obstetrics imaging. Data obtained at the time of MRI included the following: gestational age, history of fetal anomalies in previous pregnancies if present, and the US diagnosis given upon referral. MRI studies were reviewed by the radiologists in this study for the presence of fetal malformations and diagnosis was given by consensus. US images were analyzed in correlation with prenatal MRI and postnatal imaging findings. For statistical purpose, urinary abnormalities were grouped into the following: Renal (including ureters) and vesicourethral. Bilateral findings were counted separately. Brain surface coil. No patients were excluded because of contraindication to MRI or claustrophobia. Most patients were positioned supine and head first into the gantry. Patients who could not lie supine were put in the left lateral decubitus. MR imaging was obtained along fetal body planes using T2-weighted single shot fast spin echo (SSh) (TTR/TE 10,000/100 ms, 4-mm slice thickness, matrix 196 x 256 or 256 x 256) and steady state free precession sequence (TR/TE 3.5–4 ms/1.7–2 ms, FA 60–90, 1–2 signals acquired, 256 x 256 matrix, and 4 mm slice thickness with no inter-slice gap). Additional T1-weighted MR images were obtained using a breath-hold spoiled gradient echo sequence (100–140/4.2) (repetition time TR msec/echo time TE msec), 70–90° flip angle (FA), 256 x 160–256 matrix, one signal acquired, slice thickness between 4 and 6 mm with an inter-slice gap of 0.2–0.4 mm. No contrast agent, sedative, or fetal paralysis were used. All fetal MRI examinations and MR images in this study were approved at the time of acquisition by attending radiologist experienced in MRI and obstetrics imaging. Data obtained at the time of MRI included the following: gestational age, history of fetal anomalies in previous pregnancies if present, and the US diagnosis given upon referral. MRI studies were reviewed by the radiologists in this study for the presence of fetal malformations and diagnosis was given by consensus. US images were analyzed in correlation with prenatal MRI and postnatal imaging findings. For statistical purpose, urinary abnormalities were grouped into the following: Renal (including ureters) and vesicourethral. Bilateral findings were counted separately. Brain
abnormalities were grouped into the following: posterior fossa, ventricular, callosal and cerebral anomalies. Other anomalies were counted per organ.

We prospectively studied the impact of the information obtained by fetal MRI on prenatal diagnosis in consultation with the referring physicians.

2.1. The reference standards

Follow-up was done for all of the studied cases. In viable babies, the diagnosis was confirmed with clinical examination and postnatal imaging. In cases of termination of pregnancy, we offered autopsy. If the parents did...
not permit autopsy, we offered gross pathological examination of the abortus and postmortem MRI. Retrospectively, we correlated fetal MRI findings with prenatal US findings and final diagnoses.

For statistical analysis, data were described in terms of range, mean, frequency, percentages, sensitivity and specificity when appropriate. McNemar test was used to compare proportion of abnormal findings by US and MRI as related to total abnormalities at final diagnosis.

All statistical calculations were done using the computer program SPSS (Statistical Package For The Social Science: SPSS Inc., Chicago, IL, USA) version 16 for Microsoft Windows.

3. Results

3.1. Prenatal imaging findings

We reported prenatal US and MRI findings in the studied 43 oligohydramnios singleton pregnancies in correlation with the final diagnosis as per the outcome measures.

3.2. Fate and outcome measures

We followed the fate of All of the 43 studied cases: twenty-one viable fetuses were born, three cases had spontaneous abortion shortly after MRI, and 19 cases had therapeutic abortion. Mortality rate in our study reached 51.1%. In cases of terminated pregnancies, the outcome measures included autopsy (n = 18), and postmortem MRI (n = 4). The outcome measures for viable 21 babies included clinical examination of the newborn as well as one or more of the following: postnatal abdomino-pelvic US (n = 18), abdomino-pelvic MRI and magnetic resonance urography (MRU) (n = 2), CT abdomen (n = 1), voiding cysto-urethrogram (VCUG) (n = 3), brain CT (n = 1), brain MRI (N = 16), and X-rays for the skeletal system (n = 1).

Chromosome analysis showed two cases with Trisomy 13, and the remainder cases had normal karyotype.

3.3. Final diagnoses

Outcome measures identified one normal subject and 42 malformed ones. Final diagnoses of the 43 cases – as per the involved body systems – included abnormalities of the urinary system in 36 fetuses (83.7%), brain malformations in 23 (53.5%), skeletal system in 4 (9.3%), hearts in 3 (7%), and hepatobiliary in 3 (7%). The numbers of abnormal findings per body systems at both US and fetal MRI, as well as at final diagnosis are summarized at Table 1.

3.3.1. Correlation of prenatal imaging findings of each fetal body system with the final diagnosis

3.3.1.1. Urinary system. Final diagnoses of the urinary malformations in the 36 cases included 75 abnormal findings, distributed as bilateral renal agenesis (n = 5), bilateral renal hypoplasia (n = 1), bilateral autosomal recessive polycystic kidney diseases (ARPKD) (n = 20), bilateral multicystic-dysplastic kidneys (MCDK) (n = 1), and bilateral renal enlargement associated with intrauterine cytomegalovirus (CMV) infection (n = 1), posterior urethral valve with secondary bilateral collecting system dilatation (n = 4), unilateral (n = 1) or bilateral (n = 3) urinary collecting system dilatation due to other causes.

Both prenatal US and MRI correctly diagnosed urinary malformations in 32 out of 36 fetuses. Both prenatal US and MRI correctly diagnosed: six fetuses with bilateral renal agenesis/ hypoplasia by documenting the absence/ diminished renal tissues respectively and non-filling of the urinary bladder; 20 fetuses with bilateral ARPKD appeared as enlarged kidneys with high signal intensity on T2-weighted MR images and high echogenicity on US; a fetus with bilateral renal enlargement related to CMV infection; four fetuses with posterior urethral valve (PUV) causing secondary bilateral hydrouretero-hydronephrosis, as well as dilated thick walled urinary bladder, and dilated posterior urethra appearing as ‘key-hole sign’; and a fetus with unilateral dilated collecting system caused by ipsilateral uretero-vesical obstruction.

The remaining four fetuses were missed by US, while MRI correctly added bilateral obstructive uropathy in two fetuses, and modified the diagnosis from unilateral to bilateral in another two fetuses.

The sensitivity and specificity for prenatal imaging in diagnosing urinary system malformations in the 43 oligohydramnios pregnancies were 92% and 100% for US and 100% and 100% for MRI respectively.

3.3.1.2. Brain malformations. Outcome measures identified brain malformations in 23 fetuses that included combinations of 41 findings: Dandy Walker Malformation complex (DWM) (n = 12), cerebellar hypoplasia (n = 1), posterior cephaloceles (n = 11), ventriculomegaly (n = 9), hydrocephalus with obstruction at aqueduct of Sylvius (n = 1), agenesis of corpus callosum (n = 2), alobar holoprosencephaly (n = 1), semilobar holoprosencephaly (n = 1), molar tooth sign (n = 1), anencephaly (n = 1), and compressed

Table 1

<table>
<thead>
<tr>
<th>Body system</th>
<th>No. of affected fetuses</th>
<th>No. of findings</th>
<th>No. of abnormal findings at US</th>
<th>No. of findings at fetal MRI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary</td>
<td>36</td>
<td>75</td>
<td>69 (92.0%)</td>
<td>75 (100%)</td>
<td>0.018</td>
</tr>
<tr>
<td>Brain</td>
<td>23</td>
<td>41</td>
<td>33 (80.5%)</td>
<td>41 (100%)</td>
<td>0.008</td>
</tr>
<tr>
<td>Skeletal</td>
<td>4</td>
<td>5</td>
<td>1 (20%)</td>
<td>1 (20%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Cardiac</td>
<td>3</td>
<td>6</td>
<td>6 (100%)</td>
<td>3 (50%)</td>
<td>0.50</td>
</tr>
<tr>
<td>Hepatic</td>
<td>3</td>
<td>3</td>
<td>2 (66.7%)</td>
<td>3 (100%)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

*P value < 0.05 is significant (bold), it is two tailed.
medulla oblongata caused by cranio-cervical stenosis (n = 1).

Fetal MRI correctly identified all of the brain malformations findings in the 23 fetuses. US correctly identified brain malformations in 15 fetuses, and missed findings in 8 fetuses that included combinations of posterior cephaloceles (n = 5), DWM (n = 3), cerebellar hypoplasia (n = 1), Molar tooth sign (MTS) (n = 1), compressed medulla oblongata (n = 1), and partially separated cerebral hemispheres in a fetus with US diagnosis of alobar holoprosencephaly that refined the diagnosis to semilobar holoprosencephaly. Fetal MRI correctly ruled out US-suspected posterior cephalocele in a normal fetus and agenesis of corpus callosum in another. The sensitivity and specificity for prenatal imaging in diagnosing brain malformations in the 43 oligohydramnios pregnancies were 78% and 99% for US, and 100% and 100% for MRI respectively.

3.3.1.3. Skeletal. Post-delivery/postmortem examinations identified skeletal malformations in 4 fetuses that included axial polydactyly as a component of Meckel Gruber syndrome (MKS) in 3 fetuses, as well as micromelia, and cranial cervical stenosis in a fetus with achondroplasia. Post axial polydactyly was not detected neither by prenatal US nor by fetal MRI. In an achondroplastic fetus, Fetal MRI identified the US-occult cranio cervical stenosis, while prenatal US detected and evaluated the micromelic bones better than fetal MRI did.

3.3.1.4. Cardiac. Both fetal US and MRI identified cardiac malformations in three fetuses: hypoplastic right heart, hypoplastic left heart, and a ventricular septal defect. The cardiac abnormalities were documented by autopsy. Fetal MRI diagnosed hypoplastic right heart and hypoplastic left heart abnormalities by showing imbalanced four-chamber steady state free precession (SSFP) MR images, and diagnosed ventricular septal defect (VSD) by showing a large defect in the interventricular septum in four-chamber SSFP image. However, unlike echocardiography, MRI could not assess the cardiac functions related to these malformations.

3.3.1.5. Hepatobiliary. Final diagnoses included hepatobiliary lesions in 3 fetuses with proved MKS: dilated bile ducts in two fetuses and hepatic cysts in one. Fetal MRI identified the hepatobiliary abnormalities in the three fetuses as tubular and rounded hyperintense lesions on T2-weighted images. Prenatal US identified dilated bile ducts in 2 fetuses, and missed hepatic cysts in one.

3.3.2. Correlation of prenatal imaging findings of multiple fetal body system with the final diagnosis

Twenty-two cases in this study had malformations that involved more than one fetal body system. These included urinary, brain, skeletal, and hepatobiliary (n = 3); urinary and brain (n = 14); urinary and cardiac (n = 2); brain and cardiac (n = 1); brain and skeletal (n = 1); as well as urinary, ascites, and pericardial effusion (n = 1). The association of anomalies in multiple fetal body systems suggested the diagnosis of syndromes: Meckel Gruber syndrome (MKS) in 15 fetuses and Joubert syndrome and related cerebellar disorders (JSRD) in one. Fetal MRI correctly confirmed prenatal US diagnosis of 8 out of the 15 cases with proved MKS without adding findings. In the remaining 7 cases, fetal MRI correctly detected US-occult findings (PC, DWM, and hepatic cysts) that suggested/supported MKS diagnosis.

Of the 43 oligohydramnios pregnancies, correlation of MRI diagnosis of fetal malformations with prenatal US findings – in reference to final diagnoses- resulted in 4 groups (Table 2): 1. ‘Agreed’ in 25 fetuses (58.1%): Fetal MRI correctly confirmed prenatal US diagnosis without additional findings. These cases included the following: PUV (n = 4), bilateral renal agenesis (n = 4), bilateral ARPKD (N = 4), MKS (N = 8), alobar holoprosencephaly-Trisomy 13 (n = 1), posterior cephalocele (n = 1), anencephaly (n = 1), intrauterine CMV infection (n = 1), and hydrocephalus due to aqueduct stenosis (n = 1). 2. ‘Modified’ in 14 fetuses (32.5%): Fetal MRI correctly added US-occult findings and modified prenatal diagnosis. 3. ‘Missed’ in 2 fetuses (4.7%): Fetal MRI missed correct findings detected by prenatal US. 4. ‘Mixed’ in 2 fetuses (4.7%): Fetal MRI correctly added US-occult findings but missed other findings that were correctly detected by prenatal US.

4. Discussion

Oligohydramnios refers to amniotic fluid volume that is less than expected for gestational age [8]. The condition is commonly secondary to an excess loss of fluid due to preterm rupture of membranes or reduced urine production caused by fetal anomalies and/or aneuploidy [2,8]. There was no history of preterm rupture of membranes in our study; however, fetal MRI correctly described fetal malformations in 42 fetuses while diagnosed a normal fetus with US-suspected posterior cephalocele.

In their larger series of 224 cases of oligohydramnios-associated malformation and examined by US, Stoll and colleagues found that the majority of fetal malformations involved the urinary tract; other malformations were musculoskeletal, digestive and cardiac [2]. In our series, the majority of fetal malformations involved the urinary tracts in 36 fetuses (83.7%), followed by the brains in 23 fetuses (53.5%); other fetal body systems were less commonly encountered, namely the skeletal system in 4 fetuses (9.3%), hearts in 3 (7%), and hepatobiliary in 3 (7%).
Because in the latter half of the pregnancy the amniotic fluid is primarily fetal urine, the absence of functioning renal tissues or a blockage in the fetus’ urinary tract can result in oligohydramnios [2]. In a study of 80 cases with Potter sequence caused by renal abnormalities, cystic dysplasia consisted almost half of the cases (47.5%), while obstructive uropathy (25%), and bilateral renal agensis (21.25%) came next [9]. We had similar results in our study of 36 oligohydramnios pregnancies with urinary malformations as 58.3% had cystic kidneys, 22.2% had dilated urinary system caused by obstruction, 16.7% had bilateral renal agensis/hypoplasia, and one fetus (3%) had enlarged kidneys associated with intrauterine CMV infection. Several previous reports have described the successful use of MRI in evaluating a broad spectrum of fetal urinary malformations but without specifying the presence of oligohydramnios [7,10,11]. Thus the place of fetal MRI for determination of UT malformations in the presence of oligohydramnios still needs to be defined. In our series, fetal MRI correctly identified all of the 75 urinary system malformations in 36 fetuses (100%) in contrast to 69 malformations in 32 fetuses (92%) by prenatal US, a significant difference in favor of MRI. In other words, oligohydramnios can significantly limit US assessment of fetal anatomy and malformations [5,12].

In our study, MRI documented US findings of the absence of both kidneys and non-filling of the urinary bladder in five fetuses. When bilateral, renal agensis is incompatible with life. Prenatal documentation of bilateral renal agensis supported parents’ decision to terminate pregnancy [3].

Fetal abdominal cystic masses may result from obstruction of the urinary system. The sites of obstruction can be at the pelviureteric junction (PUJ), ureterovesical (U-V) junction, and/or urethra [7,10–12]. Fetal MRI correctly diagnosed all of the 8 fetuses with urinary obstruction in this study and accurately determined the obstruction level. Owed to its large field of view, MRI helped in accurate delineation of the full extent of a hugely dilated urinary bladder (megacystis) in a fetus in this series; the presence of dilated posterior urethra (Keyhole sign) along with thickening of the urinary bladder wall helped in establishing the prenatal diagnosis of PUV in this fetus. Prune-belly syndrome can also result in hugely dilated urinary bladder that can be confused with megacystis secondary to PUV. However, unlike in PUV, megacystis in Prune-belly syndrome has thin wall and associated with stricture of the entire length of urethra and thus does not show keyhole sign [13].

Prenatal US correctly diagnosed 5 fetuses with urinary tract obstruction and misdiagnosed/missed findings in the other 3 fetuses. In a fetus, where US suspected unilateral hydronephrosis, MRI detected a dilated ureter and refined the diagnosis to hydroureret-hydronephrosis. In two fetuses, prenatal US misdiagnosed cystic abdominal masses caused by urinary obstruction as bowel obstruction. Markedly dilated urinary system may sometimes be misdiagnosed as bowel obstruction [14]. T1-weighted MR images identified normal hyperintense meconium-filled colon in these two cases that helped in ruling out the erroneous US diagnosis.

Cystic kidneys were the most common urinary malformations in this study encountered in one fetus with bilateral multicystic dysplastic kidneys and in 20 fetuses with bilateral autosomal recessive polycystic kidneys (ARPKD). Multicystic dysplastic kidney is characterized by replacement of renal parenchyma by multiple variable-sized cysts [15]. In a fetus with US diagnosis of unilateral multicystic dysplastic kidney (MCDK) in this study, MRI detected renal cysts in the other kidney and refined the diagnosis to a bilateral disease. MCDK is a distinct entity that is not usually mistaken for other renal cystic diseases [16,17]. Unlike in hydronephrosis where there is communication with the central renal pelvis, cystic changes in MCDK are non-communicating [15]. It is also important to distinguish between ARPKD and MCDK, as the recurrence risk is 25% in the former in contrast to 3% in the latter [18]. Unlike MCDK, the cysts in ARPKD are smaller in size and usually cause marked bilateral renal enlargement [19]. MRI documented US diagnosis of bilateral ARPKD in 20 fetuses in this study. Fetal MRI identified markedly enlarged kidneys with mottled high signal appearance on T2-weighted images. The innumerable small cysts are responsible for the high signal intensity appearance of ARPKD on T2-weighted fetal MRI [7,10,11]. Classically in ARPKD, both kidneys are symmetrically enlarged and equally affected by the cystic changes [20]. The occurrence of bilateral renal anomalies and oligohydramnios should initiate a search for other fetal anomalies and syndromal affection such as Meckel Gruber syndrome (MKS) [21]. MKS is a lethal autosomal recessive disorder characterized by a combination of renal cysts and variably associated anomalies of the brain, liver cysts, and polydactyly [22–31].

Previous reports have documented the association of oligohydramnios pregnancies with fetal brain malformations such as hydrocephalus, periventricular calcification, agenesis of corpus callosum, holoprosencephaly, and microcephaly [2,26,28]. Twenty-three fetuses (53.5%) in our study had brain malformations in association with oligohydramnios and included Dandy Walker Malformation complex (DWM), posterior cephalocele (PC), ventriculomegaly, hydrocephalus, agenesis of corpus callosum, holoprosencephaly, anencephaly, and molar tooth sign (MTS). MRI proved to be a valuable adjunct to US in diagnosing fetal brain abnormalities [12,32]. Fetal MRI identified correctly all of the brain malformations in 23 fetuses in this study and was significantly superior to prenatal US which correctly identified abnormalities in only 12 fetuses. Fetal MRI correctly identified US-occult findings in 11 fetuses that were mainly related to the posterior fossa, and ruled out US-suspected posterior cephalocele in a normal fetus and agenesis of corpus callosum in another.

Malformations of fetal organs other than urinary and brain were much less encountered in association with oligohydramnios in this study and included hepatobiliary abnormalities in three fetuses (7%), skeletal malformations in four fetuses (9.3%), and cardiac malformations in three fetuses (7%).

Outcome measures revealed hepatobiliary malformations in three fetuses with MKS: two fetuses had dilated bile ducts, and one had multiple hepatic cysts. Hepatobiliary malformations have been reported with MKS and
included hepatomegaly with small cysts, absent gall bladder, or dilated bile ducts [22]. Fetal MRI correctly diagnosed hepatobiliary malformations in the 3 fetuses, while prenatal US diagnosed dilated bile ducts in 2 fetuses and could not detect the hepatic cysts in the third one.

Outcome measures revealed skeletal malformations in four fetuses in this study: polydactyly in three fetuses with MKS, and a fetus with achondroplasia. Prenatal US provided detailed assessment of the skeletal system in a fetus with achondroplasia. US is the method of choice for measuring fetal long bones and recognition of prenatal-onset skeletal dysplasias using 2D and 3D imaging [33]. Unlike prenatal US, fetal MRI could not provide detailed assessment or bony measurements of the micromelic bones, but added US-occult cranio-cervical stenosis. Recent report indicated that echo planar MR imaging (EPI) can be used to image fetal bones especially when it is difficult to assess all extremities sonographically in late gestation or if the amniotic fluid is severely reduced [34]. We did not use EPI sequence in this study, but this sequence will open the door for future studies. Polydactyly was reported with 55% of MKS being typically postaxial and bilateral [21]. Polydactyly was missed by both prenatal US and MRI and were proved only by autopsy. Prenatal US can miss subtle skeletal malformations such as polydactyly in the presence of oligohydramnios likely because of the crowding effect of oligohydramnios on fetal parts [31].

Recent preliminary reports indicated that fetal cardiac MRI is feasible in evaluation of the morphology of normal and abnormal fetal hearts using the anatomical segmental approach for congenital heart diseases [35,36]. Steady State Free Precession (SSFP) MR images allowed documentation of echocardiographic findings of the structural malformations in 3 fetuses in this study with hypoplastic right heart, hypoplastic left heart and a ventricular septal defect. However, unlike echocardiography, the technique of fetal cardiac MRI in its current status could not assess cardiac function related to these malformations, as ECG-gated fetal MRI sequences are not yet available for clinical practice [36].

Twenty-two cases in this study had malformations that involved more than one fetal body system. The association of anomalies in multiple fetal body systems suggested prenatal diagnosis of MKS in 15 fetuses, Joubert syndrome and related cerebellar disorders (JSRD) in one fetus, and intrauterine cytomegalovirus (CMV) infection in one fetus.

The association of ARPKD with brain abnormalities, hepatobiliary, and/or polydactyly suggests MKS diagnosis [22]. Fetal MRI correctly suggested MKS diagnosis in 15 fetuses in this study. The incidence of MKS is estimated to be 1/13,250 in USA live births, while it is much higher in North Africa at 1/3500 [23]. The typical renal cystic pattern of ARPKD is characteristic of MKS and the diagnosis of this disorder cannot be made in the absence of these changes [24]. Although MKS has been described classically with posterior cephalocele, many authors have expressed disagreement with the idea of an obligatory cerebral abnormality due to the wide phenotypic variation of the disorder [24–27]. A wide spectrum of brain pathology has been reported with MKS [28]. Posterior cephalocele (PC) was the most consistent malformation reported with MKS (60–90%) [29]. DWM was also accepted as part of MKS syndrome [30]. Other reported brain abnormalities with MKS included cerebral ventriculomegaly, agenesis of corpus callosum, absent olfactory bulb, fused thalami, holoprosencephaly, hypoplasia of optic nerves-chiasm, absent pituitary gland, and microcephaly [28]. Out of 15 fetuses with MKS diagnosis in our study, fetal MRI correctly identified PC in 10 fetuses (66.6%), DWM in 11 (73.3%), cerebral ventriculomegaly in 9 (60%), agenesis of corpus callosum in 2 (13.3%), and hepatobiliary dilatation/cysts in 3 (20%). MRI correctly confirmed prenatal US diagnosis of MKS in 8 out of the 15 fetuses without adding findings. In the remaining 7 fetuses, fetal MRI correctly detected US-occult findings (PC, DWM, and hepatic cysts) that suggested/supported MKS diagnosis.

In this study, fetal MRI identified US-occult malformation of the posterior fossa consistent with molar tooth sign (MTS) in association with bilateral ARPKD. MTS is a pathognomonic sign for Joubert Syndrome and Related cerebellar disorders, and it consists of thick horizontally placed superior cerebellar peduncles, associated with deepening of the interpeduncular fossa and hypoplastic vermis. The possibility to identify MTS by fetal MRI has been previously reported [37]. The association of MTS with cystic dysplastic kidneys has been described with Joubert Syndrome with renal involvement. Prenatal MRI diagnosis of MTS in association with bilateral ARPKD has been reported once in the literature [38].

In association with intrauterine cytomegalovirus (CMV) infection, both prenatal US and MRI identified bilateral renal enlargement associated with ascites and pericardial effusion in a fetus at 23 weeks of gestation. CMV infection is the most common cause of congenital infection with an annual frequency of 0.5–2.5% of live births. Oligohydramnios and fetal ascites have been described in association with intrauterine CMV infection [39]. Choong and colleagues described prenatal US findings of bilateral renal enlargement in association with intrauterine CMV infection in a fetus at 28 weeks’ gestation [40]. We correlated the overall prenatal US and MRI diagnoses of fetal malformations in the 43 oligohydramnios pregnancies with the final diagnosis.

Fetal MRI confirmed US diagnosis of fetal malformations in 25 fetuses (58.1%) that included mainly the urinary system and brain.

Fetal MRI added US-occult findings that correctly changed or modified prenatal US diagnosis in 14 fetuses (32.5%). Fetal MRI correctly diagnosed one normal fetus with US-suspected posterior cephalocele and detected US occult findings that were mostly related to the brain and/or urinary system in 13 fetuses. In two fetuses with obstructive uropathy, fetal MRI identified the dilated urinary systems and ruled out incorrect US diagnosis of colon abnormality. MRI changed US diagnosis from hydronephrosis to hydroureteronephrosis in one fetus and from unilateral multicystic kidney to bilateral multicystic kidneys in another. Fetal MRI added cerebellar hypoplasia to a correct US diagnosis of bilateral renal agenesis in one fetus. Fetal MRI added findings of brain malformation to US diagnosis of bilateral ARPKD that suggested/confirmed the diagnosis of MKS in 7 fetuses and JSRD in one fetus.
MRI missed fetal abnormalities that were detected by US and involved cardiac function of heart anomalies in 2 fetuses (4.7%). MRI missed data correctly detected by US while added US-occult findings in 2 fetuses (4.7%). In one fetus, fetal MRI identified partially separated cerebral hemispheres and modified US diagnosis of lobar holoprosencephaly to semilobar but could not assess cardiac functions related to an associated VSD. Unlike US, MRI could not fully assess the micromelic bones in a fetus with achiondroplasia, but identified cranio cervical stenosis and posterior fossa abnormalities that were US-occult.

Identification of fetal abnormalities and associated conditions is important for fetal prognosis and genetic counseling [1]. Knowledge of the fetal chromosome constitution in the setting of abnormal prenatal imaging findings has important benefit on diagnosis and counseling in oligohydramnios pregnancies [2]. Among 224 oligohydramnios pregnancies associated with fetal malformations studied by Stoll and colleagues, 13.8% had a chromosomal abnormalities. Two out of the 42 oligohydramnios pregnancies associated with fetal malformations in our study had chromosomal abnormalities. The use of fetal chromosome analysis and careful imaging examination is advised in every pregnancy complicated by oligohydramnios [2,5].

The degree of confidence required for prenatal diagnosis is clearly higher in cases where termination of pregnancy is considered. The results of fetal MR imaging in this study, whether excluding or confirming sonographically detected abnormalities, or discovering additional abnormalities that were not apparent by US, have been shown to help reach a more confident prenatal diagnosis and support counseling of the referring physicians and parents. However, management decision is multi-factorial, including the gestational age at diagnosis, the severity and type of the abnormality, the presence of multiple anomalies, as well as social and religious views [8]. In addition, the decision in pregnancy management depends also on other oligohydramnios-related deformations such as pulmonary deformity/hypoplasia which were out of the scope of this study.

A partial limitation of this study is the relatively small sample size. However, this study opens the door for further prospective works to evaluate the diagnostic ability and accuracy of MRI findings in fetal malformations associated with oligohydramnios pregnancies, a well-known US limitation.

5. Conclusion

Fetal MRI is a valuable adjunct to US in evaluating suspected fetal malformations associated with oligohydramnios specifically those related to the brain and urinary system. Fetal MRI may add findings that can modify prenatal US diagnosis and support pregnancy counseling. On the other hand, US seems to excel MRI in detection of fetuses with skeletal anomalies or cardiac functions related to heart anomalies.

Conflict of interest

Author states that there is no conflict of interest.

References


