Prenatal Ultrasound Diagnosis of Fetal Urogenital Anomalies

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ABSTRACT

Congenital urogenital anomalies constitute approximately 20 to 30% of all malformations identified in the antenatal period. Since fetal urogenital malformations are a significant cause of neonatal and child morbidity and mortality, the necessity of providing the correct diagnosis for the parents and professionals involved in the management should be of great priority.

Here, we present a review of the most common fetal urogenital malformations with special consideration of ultrasound features and addition of our ultrasound assessments.

Keywords: Autosomal dominant polycystic kidney disease, Urogenital anomalies, Ultrasound diagnosis.

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INTRODUCTION

The prevalence of fetal malformation is relatively high, with an average prevalence of 2.0%. Among all the malformations, anomalies of the urogenital tract seem to be among the most common, with a prevalence rate of 0.5 to 0.8% in unselected population according to the literature. If certain organs are considered, then kidney is the most affected site of congenital abnormalities. Since most of the parts of urogenital system can be visualized by ultrasound as early as 12 weeks of gestation and with more confidence later through pregnancy, these anomalies constitute approximately 20 to 30% of all malformations detected in the antenatal period.

Urogenital malformations can be unilateral or bilateral, mild, and asymptomatic, while in some cases can result in impaired renal function and be lethal in prenatal or postnatal period.

Additionally, these disorders predispose an individual to many other complications, such as ureteral obstruction, stone formation, infection, hypertension, renal failure, and cardiovascular disease throughout life. Although congenital anomalies of the urinary and genital tracts are a part of many known syndromes, nonsyndromic cases are probably caused by single-gene defects and are more common in families with previously affected member. Since these congenital disorders are responsible for 30 to 50% of cases of end-stage renal disease in children, it is of crucial importance to diagnose these anomalies in order to initiate therapy as soon as possible to minimize renal damage and to prevent or delay the onset of kidney failure. In case of lethal form of congenital kidney disease, it is important to diagnose it in order to give accurate information to the parents and to provide them with proper genetic counseling.

Although prenatal genetic and molecular testing of the different fetal and placental tissues has enabled a huge step-up in antenatal diagnosis of different anomalies of urogenital tract, ultrasound still remains an irreplaceable tool in initial assessment of fetal morphology. With the development of new ultrasound technologies, such as high-definition ultrasound, the diagnosis of different urogenital anomalies has moved from the second to the first trimester, enabling faster diagnosis and the possibility to perform invasive procedures earlier in pregnancy if necessary. The finding of different urogenital anomalies should be followed by detailed examination of entire fetal anatomy and evaluation of the amniotic fluid level. The differential diagnosis should take into account personal and family history, the presence of associated anomalies, karyotype, and genetic testing if available.

Here, we present a review of the use of ultrasound in the detection of fetal urogenital system with special consideration in kidney malformations since it is the most common site of different developmental disruptions.

ANOMALIES OF THE FETAL KIDNEY

Human kidney develops in early embryonic stage and it evolves through three developmental stages: Pronephros, mesonephros, and metanephros. The earliest stage is the pronephros that develops from the 4th to the 14th somites and consists of 6 to 10 pairs of tubules. These tubules join into a pair of primary ducts that grow caudally, and eventually terminate into the cloaca. The pronephros is a temporary structure that disappears completely by the
Development of the new ultrasound technologies and improvement of the resolution of the ultrasound picture enabled the earlier visualization of fetal kidneys even at the end of the first trimester. In most of the cases, kidneys can be assessed from the 9th week of gestation, while the period beyond 12 weeks should provide us with the clear demonstration. During detailed morphologic examination at the 20 gestational weeks in 95% of fetuses' kidneys should be assessed by ultrasound in detail and analyzed in their number, position, measurements, echogenic appearance. An indirect sign of renal appearance is the presence or absence of renal arteries that could be examined by color Doppler flow imaging, while the evaluation of the amniotic fluid index gives additional information about the function of the kidney. In normal circumstances ureters are not visible, while their ultrasound appearance should be followed by the detailed examination of the rest of the urogenital and other system anatomy.

The most common renal abnormalities diagnosed prenatally by ultrasound are hydronephrosis caused by transient urine flow impairment at the level of the pelvis–ureteric junction and vesico–ureteric junction or posterior urethral valve. In most cases, hydronephrosis is caused by transient urine flow impairment at the level of the ureters are not visible, while their ultrasound appearance. An indirect sign of renal appearance is the presence or absence of renal arteries that could be examined by color Doppler flow imaging, while the evaluation of the amniotic fluid index gives additional information about the function of the kidney. In normal circumstances ureters are not visible, while their ultrasound appearance should be followed by the detailed examination of the rest of the urogenital and other system anatomy.

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it has low sensitivity for individuals younger than 30 years.\textsuperscript{14} With the technological improvement of ultrasound, the prenatal diagnosis of ADPKD is now being reported with increasing frequency. Main sonographic findings of the condition are moderate renal enlargement with hyperechogenic renal cortex and hypoechochogenic medulla resulting in increased corticomedullary differentiation, while the detection of renal cysts is uncommon (Fig. 2).\textsuperscript{15} By definition, a hyperechogenic kidney is recognized as having a renal cortex more echogenic than the liver and spleen. In a case of ADPKD, amniotic fluid index is usually normal. All described ultrasound signs are not to be missed in a case of affected families; however, the signs can be neglected in a case of unexpected diagnosis.\textsuperscript{16}

Autosomal recessive polycystic kidney disease (ARPKD) is a rare autosomal recessive disorder caused by the mutation of the six chromosomes.\textsuperscript{17} In ARPKD, kidneys are usually bilaterally enlarged with many cysts due to the dilatation and elongation of renal collecting ducts. The severity of renal malformation and associated liver disease could be variable even in the same family.\textsuperscript{17} The onset of the ARPKD also varies, which represents the main criteria for the classification of ARPKD: prenatal, neonatal, infantile, and childhood form. Earlier onset of the disorder is associated with serious complications and outcome.

Prenatal ultrasound examination is a very useful imaging tool for the diagnosis of ARPKD with over 50% of cases being diagnosed prenatally.\textsuperscript{17} Although large kidneys may be visualized from 13 weeks onward, the hyperechogenicity of the kidneys that results from the presence of multiple micro cysts, dysplasia, or tubular dilatation should not be missed after 17 weeks’ gestation (Fig. 3).\textsuperscript{18} There is also an absence of corticomedullary differentiation within the kidney with decrease in amniotic fluid amount, fetal ascites, and difficulty in demonstration of fetal bladder.\textsuperscript{19} In a case of early onset of the disease, impaired renal function leads to oligohydramnios and consequently to pulmonary hypoplasia, club foot, and Potter’s faces.\textsuperscript{20} The prognosis of ARPKD is poor, with death occurring within the first two postnatal months due to the renal or respiratory failure.

Multicystic dysplastic kidney is the most frequent type of renal cystic disease, and it is one of the most common causes of an abdominal mass in infants. Multicystic
dysplastic kidney develops as an architectural disorganization due to the early obstructive defect of the branching tubules in the developing kidney. In most of the cases, this is a unilateral condition with a nonfunctional affected organ, while bilateral condition can be found in 20% of cases. About 40% of fetuses with multicystic dysplastic kidney have additional genitourinary abnormalities. Condition is usually diagnosed prenatally by ultrasound visualization of enlarged kidney, with renal cortex being replaced by numerous cysts of multiple sizes with dysplastic parenchyma and absent calyceal drainage system (Fig. 4). The parenchyma can be visualized in small islands between the cysts. Prognosis for unilateral disorder is good, while the bilateral condition, which is associated with decreased amniotic fluid level, is incompatible with life.

Solitary renal cyst is a rare condition in prenatal period and childhood. In the antenatal ultrasound assessment in the second trimester, the condition can be found with a frequency of 1 in 1,100 pregnancies (0.09%). The diagnosis of a solitary renal cyst is made when there is a single, nonseptated cyst, with well-defined borders, without communication between the cavity of the cyst and the renal collecting system, in an otherwise normal appearing kidney (Fig. 5). This condition is not usually associated with other anomalies. Solitary renal cyst has a transient nature and usually disappears by the end of the pregnancy or at early neonatal period, while persisting cysts do not increase in size and compromise renal function.

Different renal abnormalities can be found in several genetic syndromes, such as: Meckel-Gruber, Bardet-Biedel, and Beckwith-Wiedemann. Meckel-Gruber syndrome is a rare autosomal recessive lethal condition. The anomalies within the syndrome can be variable but the most common are dysplastic kidneys, olygohidramnios, occipital encephalocele, postaxial polydactyly, and limb shortening. Dysplastic kidneys consist of multiple microscopic cysts that destroy the tissue and increase the kidneys in size for more than 10 to 20 times, resulting in nonfunctional organs and decreased amount of amniotic fluid. Common ultrasound findings are enlarged kidneys containing cysts that increase in size toward the medulla with olygohidramnios (Fig. 6). The mean prevalence of...
Meckel-Gruber syndrome in Europe is 2.6 per 100,000 births in a subset of registries with good ascertainment, but there are differences between the regions.24

Bardet-Biedel syndrome is a ciliophatic genetic disorder that can affect various organs and systems in a human body. It has different expressivity and a wide range of clinical variability even within the same family. The most common clinical features are truncal obesity and urogenital malformations, such as ectopic urethra, uterus duplex, septate vagina, retinitis pigmentosa, and polydactyly. Many of the children that survive the infancy suffer from developmental delay, speech disorder, and mental retardation. Prenatal diagnosis of Bardet-Biedel syndrome is complicated since the main findings are nonspecific, such as enlarged, echogenic kidneys with decreased amniotic fluid levels (Fig. 7). Finding of other additional anomalies can help the professional to establish the diagnosis. This disorder is inherited in autosomal recessive pattern with prevalence of 1 in 140,000 to 1 in 160,000 of the newborns.25

Beckwith-Wiedemann syndrome appears in sporadic manner, but there are certain families with several affected members. The prevalence of this disorder is estimated to be 1 in 15,000 live births.26 The syndrome can be described as an overgrowth disorder usually present at birth, characterized by an increased risk of childhood cancer and certain congenital features. The diagnosis of Beckwith-Wiedemann syndrome was typically made after birth until Williams and coworkers published guidelines for the prenatal diagnosis of this condition.26 They proposed schema of two major criteria (abdominal wall defect, macroGLOSSia, macrosomia) or one major plus two minor criteria (nephromegaly/dysgenesis, adrenal cytomegaly, aneuploidy/abnormal loci, polyhydramnios) for prenatal diagnosis of Beckwith-Wiedemann syndrome. Common ultrasound picture of the kidneys in Beckwith-Wiedemann syndrome includes enlarged organs with enhanced echogenicity accompanied by the normal or increased amount of the amniotic fluid (Fig. 8). Children with this syndrome are at higher risk to develop cancer during childhood, particularly Wilms’ tumor (nephroblastoma), pancreatoblastoma, and hepatoblastoma, but do not have an increased risk of developing cancer in adulthood. In general, the prognosis is very good since most children with Beckwith-Wiedemann syndrome do not develop cancer and the vast majority of children who do develop cancer can be treated successfully.

Since most of the syndromes with renal involvement are autosomal recessive and relatively uncommon, the diagnosis could be hard to reach and recurrence may be difficult to predict. In any way, professional must try hard to provide the diagnosis due to its serious implications in the continuation or termination of pregnancy, evaluation of possible affection of other family members, and genetic counseling for the family. Although precise prenatal diagnosis of different kidney disease can be made using genetic testing of different fetal and chorionic materials, these methods are quite expensive and often unavailable in everyday practice so ultrasound evaluation remains the most widely used technique for diagnosis of different congenital kidney disorders. Although prenatal ultrasound assessment is an efficient method to examine renal anatomy, it has certain limitations in assessing renal function. Useful parameters can be amniotic fluid volume and echogenicity of renal parenchyma, both of which can be used as indicators of the underlying renal reserve. In better-equipped perinatal centers, ultrasound findings of different kidney anomalies can be followed by magnetic resonance imaging (MRI).

ANOMALIES OF THE FETAL BLADDER

By the end of the 7th gestational week the embryo has a cloaca, which is a single cavity at the caudal end of the
body. After that stage, the cloaca divides into two parts; ventral part that becomes the primary urogenital sinus and dorsal part that develops into the rectum. The urogenital sinus will further be subdivided into the cranial portion, which will form the future urinary bladder, while the caudal part will give the basis for future prostate, urethra, and external genitalia portions. Congenital anomalies of the lower urinary tract are a significant cause of neonatal morbidity and mortality in infancy so it is of great importance to diagnose these anomalies if possible in the antenatal period to provide the neonates timely set management and surgical treatment.

One of the most common congenital obstructive lesions of the urethra is posterior urethral valve that occurs only in phenotypic boys. This anomaly results from the formation of a thick membrane from the tissue of wolffian ducts. Posterior urethral valve can cause renal damage in children with end-stage renal disease in a subsequent proportion of children. The severity of the anomaly can be different depending on the various degrees of the obstruction within the urethra.27 Ultrasound manifestations of the posterior urethral valve can be different due to the severity of the anomaly. In most severe cases, fetus will be small for gestational age with oligohydramnios. The signs of the lower urinary tract indicative for posterior urethral valve are a keyhole sign, which is actually the combination of the bladder distention and upper part of the urethra immediately proximal to the valve together with the hypertrophy of the bladder wall. Additional findings can be hydronephrosis and hydroureter with different degrees of kidney dysplasia. It is important to stress out that all of these ultrasound features start to be visible from 26 weeks of the gestation onward, making hard to identify posterior urethral valve on routine detailed ultrasound examination usually carried out at 18th week.28 Less severe cases are usually detected in postnatal period due to the repeated urinary infections.27

Cloacal malformations are rare congenital malformations that present only in phenotypic girls as remain of the structure from an early embryonic state. Cloacal malformations develop as a result of the disrupted division of the cloaca in the rectum and urogenital sinus, resulting in one common perineal opening for the urinary, genital, and gastrointestinal tracts, while the abdominal wall remains normal.29 Prenatal diagnosis based on the ultrasound can be hard to achieve due to the unexpected diagnosis and nonspecific ultrasound appearance of the anomaly. Most common sonographic findings are: Abdominal/pelvic cystic/mass, hydronephrosis, oligohydramnios, distended bowel/bowel obstruction, ascites, two-vessel cord, and dilated bladder.30 One should suspect the diagnosis of cloaca in a case of cystic abdominal masses with the combination of gastrointestinal and urological abnormalities in female fetus. Surgical management of the anomaly is pretty complicated, while the functional prognosis of individuals born with cloacal malformations with regard to achieving fecal and urinary continence is different depending on the complexity of the defect and the status of the spine and sacrum.

Bladder exstrophy is a rare congenital anomaly characterized by the protrusion of the urinary bladder through a defect in the abdominal wall. It can occur in both female and male fetuses with low incidence of about 1 in 10,000 to 1 in 50,000 of all pregnancies with higher incidence in females.31 This malformation is considered to be the result of cloacal division and is usually combined with the abnormalities of the bony pelvis, pelvic floor, and genitalia. Ultrasound features of urinary bladder exstrophy include normal amniotic fluid index with normal kidney appearance, while bladder could not be visualized. Additional findings are low insertion of the umbilical cord and defect of the anterior abdominal wall in the portion below the umbilicus.32 The prognosis for urinary continence is usually good after surgical correction but it depends upon other system anomalies.

ANOMALIES OF THE FETAL GENITAL TRACT

The most common anomaly of the fetal genital tract seen on ultrasound is ovarian cyst in female fetuses. It is also the most common intra-abdominal mass found by antenatal ultrasound in females.33 A fetal ovarian cyst can be of variable size and usually detected in the third trimester. It is believed that their occurrence is related with the action of different hormones of maternal and placental origin, such as estrogen and beta-human chorionic gonadotropin. Ultrasound appearance of the cyst is a well-circumscribed anechoic, unseptated cyst in the fetal pelvis separate from the fetal bladder, stomach, and gall bladder, which does not change its dimensions through pregnancy.33 These cysts are usually simple and uncomplicated with good prognosis and spontaneous resolution. Possible complications are rare, but include torsion, hemorrhage, and rupture.

Although external genital abnormalities are quite rare, the latest improvement of ultrasound technology, such as three- and four-dimensional high-definition (HD) ultrasound has enabled more precise assessment of genital organs and the correct establishment of the diagnosis in a case of malformations.

CONCLUSION

Ultrasound assessment through the pregnancy continues to be the most important source of clinical information in the evaluation of urogenital tract disorders. Additional
molecular and genetic testing can be helpful in the process of diagnosis determination but are often unavailable and expensive with the lack of utility in a case of multifactorial disorders. Since fetal urogenital malformations are a significant cause of neonatal and child morbidity and mortality, the necessity of providing the correct diagnosis for the parents and professionals included in the management should be of great priority for the obstetricians dealing with ultrasound examination.

REFERENCES