Antenatal assessment of kidney morphology and function.

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1- INTRODUCTION

Today, in many European countries, three obstetrical ultrasound (US) examinations are performed, one in each trimester (1). In other countries, including the United States and Canada, only a second-midtrimester examination is performed routinely; with first-trimester or third-trimester examinations performed only when there is a specific indication (2). The more systematic use of obstetrical US has led to the discovery of many fetal abnormalities, among which the congenital abnormalities of the kidney and urinary tract (CAKUT) make up one of the largest groups of congenital anomalies amenable to neonatal care, representing 0.2 to 2% of all newborns (1). Perhaps the addition of three-dimensional US scanning and magnetic resonance imaging (MRI) may improve the ability to detect and define these abnormalities (3). In addition, nowadays CAKUTs are mostly found in asymptomatic patients and the treatment applied is mainly preventive (4, 5, 6).

2- THE NORMAL URINARY TRACT

2-1 Bladder

Urine starts to be produced during the ninth week of fetal life and at that time, the bladder can be visualized as a fluid-filled structure within the fetal pelvis. During the second and third trimester, the fetus normally fills and partially or completely empties the bladder approximately every 25 minutes and the cycle can be monitored during the sonographic examination (7).

2-2 Kidneys

During the first trimester, the kidneys appear as hyperechoic oval structures at both sides of the spine (8). This echogenicity will progressively decrease. During the third trimester the cortical echogenicity will always be less than that of the liver or spleen. Simultaneously with the decrease of echogenicity, corticomedullary differentiation will

appear around 14 to 15 weeks. It should always be demonstrated in fetuses older than 18 weeks (Figure 1).

Growth of the fetal kidneys can be evaluated throughout pregnancy. As a rule, a normal kidney grows at about 1.1 mm per week of gestation.

2-3. Evidence of normally functioning urinary tract

Besides visualization of the bladder and normal kidneys, assessment of the urinary tract should include an evaluation of the amniotic fluid volume. After 14 to 15 weeks, two thirds of the amniotic fluid is produced by fetal urination and one third by pulmonary fluid. A normal volume of amniotic fluid is mandatory for proper development of the fetal lungs. This can be confirmed by measuring thoracic diameters or thoracic circumference (9).

3- ULTRASOUND FINDINGS AS EVIDENCE OF ABNORMAL FETAL KIDNEY AND URINARY TRACT.

Anomalies of the urinary system detected in utero are numerous (10, 11); they can include anomalies of the kidney itself, of the collecting system, of the bladder and of the urethra. In addition, they can be isolated or in association with other systems. Therefore, the sonographic examination should be as meticulous as possible in order to visualize the associated features. These findings, among others, will determine the prognosis.

3-1 Abnormal renal number

The diagnosis of bilateral renal agenesis is based on the absence of renal structure and the presence of oligohydramnios after 15 weeks of gestation. Pulmonary hypoplasia is invariably associated and leads to death from respiratory failure soon after birth. In this context, enlarged globular adrenals should not be mistaken for kidneys (12). The use of color Doppler may help demonstrate the absence of renal arteries and subsequently confirm the diagnosis (13).

Unilateral renal agenesis is more common (1 in 500 pregnancies) and usually has no significant consequence on postnatal life. The pathogenesis of renal agenesis is mostly failure of formation of the metanephros, interruption in vascular supply or regression of a multicystic dysplastic kidney (MCDK) (14). An investigation after birth is necessary to confirm the status of the remnant kidney and to look for possible associated anomalies (15). It is obvious that children having ipsilateral uronephropathy are at higher risk of adverse outcome, with a median time to chronic kidney disease of 14.8 years (16).

3-2 Abnormal renal location

Ectopic kidney, especially in the pelvic area, is common (15). The diagnosis of horseshoe or crossed fused kidneys can also be assessed in utero thanks to the demonstration of a typical corticomedullary differentiation (17). An ectopic kidney is usually small and somewhat malrotated. Ectopic kidneys may be asymptomatic, but complications from ureteral obstruction, infection, and calculi are common. Therefore, in complex cases, the anomaly has to be confirmed after birth by US and voiding cystourethrography (VCUG).

3-3 Abnormal renal echogenicity

Hyperechogenicity of the fetal kidney is defined by comparison with the adjacent liver or spleen. The kidney is "physiologically" hyperechoic (or isoechoic at the end of the second trimester). It is easier to characterize after 28 to 32 weeks when the renal cortex should be hypoechoic compared to the liver and spleen (8). Increased echogenicity of the renal parenchyma may occur as a response to different changes in renal tissue (18). Interstitial infiltration, sclerosis and multiple microscopic cortical and medullary cysts may account for hyperechogenicity even in the absence of macrocysts. The detection of hyperechoic kidneys represents a difficult diagnostic challenge (19). The differential diagnosis must be based on kidney size, corticomedullary differentiation, the presence of macrocysts, the degree of dilatation of the collecting system and the amount of amniotic fluid (20, 21). The diagnosis

must also take into account the familial history and the presence of associated anomalies. So far, the outcome of fetal hyperechoic kidneys can only be predicted accurately in severe cases with significant oligohydramnios (19, 21). It should be stressed that some cases remain unsolved and have to be considered as normal variants (21). Table 1 provides information on the spectrum of renal disorders associated with fetal hyperechoic kidneys.

3-4 Abnormal renal size

Measurements of the kidneys must be systematic whenever an anomaly of the urinary tract or amniotic fluid volume is suspected. It is therefore important to have standards for renal size and volume measurements covering the complete gestational age range, because renal pathology often presents late in pregnancy (22). Small kidneys most often correspond to hypodysplasia or damaged kidneys from obstructive uropathy or high-grade vesicoureteral reflux (VUR) (23, 24). Enlarged kidneys may be related to urinary tract dilatation, renal cystic diseases, fetal overgrowth disorders (Beckwith-Wiedemann syndrome) or tumoral involvement.

3-5 urinary tract dilatation

Fetal renal pelvis dilatation is a frequent abnormality that has been observed in 4.5% of pregnancies (25). Pyelectasis is defined as dilatation of the renal pelvis whereas pelvicaliectasis and hydronephrosis include dilatation of calyces. In practice, these terms are interchanged and used as descriptions of a dilated renal collecting system regardless of etiology (26).

The third-trimester threshold value for the anteroposterior (AP) renal pelvis diameter of 7 to 10 mm is certainly the best prenatal criterion both for the screening of urinary tract dilatation and for the selection of patients needing postnatal investigation (22, 25).

There are several theories that account for the visibility of the renal pelvis during pregnancy. The distension of the urinary collecting system may be simply a dynamic and

physiologic process (27, 28). The tendency of renal pelvis dilatation to resolve spontaneously is supported by normal postnatal renal appearances reported in 36 to 80% of cases followed up after birth (29, 30). However, prenatally detected renal pelvis dilatation may be an indicator of significant urinary tract pathologies (31). The likelihood of having a clinically significant uropathy is directly proportional to the severity of hydronephrosis (26). A summary of the literature describing the postnatal uronephropathies found in neonates who presented with fetal renal pelvis dilatation is given in table 2. The two main pathologies found are pelviureteric junction stenosis and VUR. US is the first examination to perform after birth (35). In babies with fetal renal pelvis dilatation, the presence of persistent renal pelvis dilatation or other ultrasonographic abnormalities (such as calyceal or ureteral dilatation, pelvic or ureteral wall thickening and absence of the corticomedullary differentiation) and signs of renal dysplasia (such as small kidney, thinned or hyperechoic cortex or cortical cysts) should determine the need for further investigations (36, 37). Based on our own experience (29, 36, 38), we propose an algorithm for a rational postnatal imaging strategy (Figure 2). Using this algorithm, we found that very few abnormal cases escaped the work up and that the risk of complications was very low.

3-6 Renal cysts

Renal cystic diseases should be suspected not only in the case of obvious macrocysts but also in the case of hyperechoic kidneys (24). Cysts may be present in one or both kidneys. Their origin may be genetic, and they may occur as an isolated anomaly or part of a syndrome. Familial history is of great importance for the diagnosis (39).

Obstructive renal dysplasia and MCDK are the most common entities in which macrocysts can be detected. Obstructive renal dysplasia is associated with urinary tract obstruction that may have resolved at the time of diagnosis, leaving the cystic sequelae behind as the sole evidence that urinary flow impairment ever existed (8). In this condition, the cysts

measure less than 1 cm and are located within the hyperechoic cortex (20). MCDK is discussed further under Renal Causes of Fetal Renal Abnormalities in this article. Although rare, isolated cortical cysts may be seen in utero. They may persist after birth or regress spontaneously (40).

The most frequent genetically transmitted cystic renal diseases are the autonomal recessive and dominant polycystic kidney diseases (also discussed under Renal Causes of Fetal Renal Abnormalities).

Abnormalities of the hepatocyte nuclear factor-1β (HNF1B) encoded by the *TCF2* gene are typically associated with bilateral cortical renal microcysts and also with other renal parenchymal abnormalities including MCDK and renal dysplasia (41, 42). Both the type and the severity of the renal disease are variable in children with HNF1B mutations: from severe prenatal renal failure to normal renal function in adulthood. There is no obvious correlation between the type of mutation and the type and/or severity of renal disease. Furthermore, the inter- and intrafamilial variability of the phenotype in patients who harbor the same mutation is high, making the genetic counseling particularly difficult in these families (43).

Cystic kidneys are also part of many syndromes (Tables 1 and 3) that present many associated anomalies that are sometimes typical of the underlying pathology.

3-7 Renal tumors

Fetal renal tumors occur only rarely. Mesoblastic nephroma represents the most common congenital renal neoplasm (52). It is a solitary hamartoma with a usually benign course. Mesoblastic nephroma appears as a large, solitary, predominantly solid, retroperitoneal mass arising and not separable from adjacent normal kidney. It does not have a well-defined capsule and may sometimes appear as a partially cystic tumor (8). It frequently coexists with polyhydramnios although the reason for this association remains unclear (52). Wilm's tumor is exceptionally rare in the fetus and may be indistinguishable from mesoblastic

nephroma on imaging (53). Another differential diagnosis to include is nephroblastomatosis, which appears either as hyperechoic nodule(s) or as a diffusely enlarged hyperechoic kidney (54). Renal tumors have to be differentiated from adrenal tumors and from intra-abdominal sequestrations (55).

3-8 Bladder abnormalities

In the setting of oligohydramnios, nonvisualization of the bladder after the tenth week of gestation indicates strong evidence of bilateral severe renal abnormality with decreased urine production.

Nonvisualization of the bladder with an otherwise normal sonogram (kidneys and amniotic fluid) may be due to physiologic bladder emptying cycle in the fetus. Normal repletion should be checked within the following 20 minutes. Persistent absent bladder can be due to its inability to store urine in cases of bladder or cloacal extrophy (56). In this context, no bladder is seen between the two umbilical arteries. Bladder extrophy or cloacal malformations represent a diagnostic challenge on US; MRI may help to precise the pelvic anatomy of the fetus (57).

Enlarged bladder in the first trimester is of poor prognosis. Most of the cases are secondary to urethral atresia or stenosis, some are syndromal (such as Prune Belly), or associated with chromosomal anomalies. Later in pregnancy, megabladder is defined as a cephalo-caudal diameter superior to 3 cm in the second trimester and to 5 cm in the third trimester. Megabladders are mainly due to outflow obstruction or to major bilateral reflux (58). The prenatal differentiation between both is often difficult because the two entities may be associated. An irregular and thickened bladder wall is suggestive of an outflow obstruction. Megacystis-microcolon hypoperistalsis (MMH) syndrome is one of the differential diagnoses that carries a very poor prognosis (59). MR can exclude it thanks to the good visualization of the colon in the third trimester.

4- ASSESSMENT OF FETAL RENAL FUNCTION.

In utero, excretion of nitrogenous waste products and regulation of fetal fluid and electrolytes balance as well as acid-base homeostasis are maintained by the interaction of the placenta and maternal blood (60). Since fetal homeostasis depends on the integrity of the placenta, it is very difficult to assess the functional status of the fetal kidney. Furthermore, changes in the volume or composition of fetal urine may in many instances reflect the condition of the placenta rather than the condition of the fetal kidney (61). However, exact diagnosis of renal abnormalities and accurate prediction of the renal function after birth are important tasks, because different renal diseases may require different approaches and therapies. Therefore, in addition to using fetal renal sonography to determine potential fetal renal anatomical abnormalities, one must be able to assess function as accurately as possible.

4-1 Amniotic fluid volume

During the first trimester of gestation the placenta (chorion and amniotic membrane) is the principal source of amniotic fluid, but after 15 weeks fetal kidneys produce the majority of amniotic fluid. Therefore, the assessment of the quantity of amniotic fluid after 15 weeks constitutes the initial step in the evaluation of the fetal urinary tract. Abnormal amounts of amniotic fluid must alert the sonographer to search diligently for renal and urinary tract anomalies (62). Assessing amniotic fluid volume is difficult and mostly subjective. However, the four-quadrant sum of amniotic fluid pockets (amniotic fluid index) provides a reproducible method for assessing amniotic fluid volume with interobserver and intraobserver variation of 3% to 7% (63).

Various cut-off criteria have been suggested for definition of oligohydramnios by amniotic fluid index, including less than 1st percentile (64), or 5th percentile for gestational age (63). Oligohydramnios of any cause typically compresses and twists the fetus, thus leading to a recurrent pattern of abnormalities that has been called the oligohydramnios

sequence (16). Oligohydramnios may be caused by decreased production of fetal urine from bilateral renal agenesis or dysplasia, or by reduced egress of urine into the amniotic fluid due to urinary obstruction. Other causes may be fetal death, growth retardation, rupture of the membranes, or post-term gestation (Table 4).

In cases of bilateral obstructive uropathy, Zaccara et al. found the evaluation of amniotic fluid by the amniotic fluid index to be the most reproducible and inexpensive method to predict renal function after birth (65).

Finally, one of the most devastating consequences of oligohydramnios, especially before 24 week's gestation, is pulmonary hypoplasia (9). Traditional explanations suggest that oligohydramnios causes pulmonary hypoplasia either by compression of the fetal thorax (66) or by encouraging lung liquid loss via the trachea (67). However, since several morphogenetic pathways governing renal development are shared with lung organogenesis, this sequence is put into question. Some reports suggest that abnormal lung dysplasia may precede the advent of oligohydramnios in fetuses with intrinsic defects of renal parenchymal development (68).

Polyhydramnios is defined as a high level of amniotic fluid. Because the normal values for amniotic fluid volumes increase during pregnancy, this definition will dependent on the gestational age of the fetus. During the last 2 months of pregnancy, polyhydramnios usually refers to amniotic fluid volumes greater than 1,700 to 1,900 ml. Severe cases are associated with much greater fluid volume excesses. The two major causes of polyhydramnios are reduced fetal swallowing or absorption of amniotic fluid and increased fetal urination (Table 4). Increased fetal urination is typically observed in maternal diabetes mellitus, but it may be associated with fetal renal diseases as mesoblastic nephroma (52), Bartter syndrome (69), congenital nephrotic syndrome (70) and alloimmune glomerulonephritis (71).

4-2 Fetal urine biochemical markers

Fetal urine biochemistry was introduced about 30 years ago as an additional test to improve prediction of perinatal death and renal failure at birth (72). Thereafter, investigators started to establish reference ranges with gestation for different biochemical parameters of fetal urine (73). Fetal urine biochemistry is currently used especially in dilated uropathies because of technical difficulties of sampling fetal urines from a nondilated urinary tract, as seen in the majority of nephropathies. Sodium is the most widely used fetal urinary marker, although other compounds such as calcium, chloride, β2-microglobulin and cystatin C may be also of interest; prognostic values of these markers are outlined in table 5. Most studies related to analysis of fetal urine agree on some points (78): 1) Fetuses with renal damage (dysplasia) show increased urinary concentrations of solutes; 2) urinary sodium and calcium yield the best accuracy among measurable electrolytes; 3) β2-microglobulin and cystatin C allow better accuracy than the measurement of any single electrolyte; 4) the accuracy of the proposed parameters are, however, far from being perfect.

4-3 Fetal blood sampling

Fetal blood sampling probably poses greater risks than urine sampling, but it allows measurement of a better index of fetal glomerular filtration rate (GFR) (78-80). In the fetus, creatinine cannot be used as a marker of GFR because it crosses the placenta and is cleared by the mother. This is not the case with α1-microglobulin, β2-microglobulin and cystatin C, which have been used to predict renal function in uropathies and nephropathies (Table 6). This technique may be helpful, especially in cases where fetal urine is difficult to sample. It is however unlikely that fetal serum α1-microglobulin, β2-microglobulin and cystatin C will overcome the limitations associated with fetal urinalysis (79). The only take-home message of clinical interest would be that fetal serum β2-microglobulin remains the best marker of renal function (less than 3.5 mg/L good outcome; more than 5 mg/L poor outcome) (81).

4-4 Ultrasound-guided renal biopsies

Although ultrasound-guided renal biopsy would theoretically allow precise definition of the extent of renal damage in obstructed and primarily dysplastic kidneys (82), this approach is limited by its invasiveness and high rate of failure in obtaining an adequate sample (78).

5- SPECIFIC RENAL AND URINARY TRACT PATHOLOGIES

Causes of fetal abnormalities of the kidney and urinary tract may be considered as prerenal, renal and postrenal.

5-1 Pre-renal causes of fetal renal abnormalities

5-1-1 Intrauterine growth restriction (IUGR)

The cause of IUGR is multifactorial. Worldwide, maternal nutritional deficiencies and inadequate uteroplacental perfusion are among the most common causes of IUGR.
IUGR caused by placental insufficiency is often associated with oligohydramnios due to reduced urine production rate in these fetuses. This phenomenon is probably due to chronic hypoxemia that leads to the brain-sparing redistribution of oxygenated blood away from non-vital peripheral organs such as the kidneys (60). As a consequence, fetal renal medullary hyperechogenicity may develop between the twenty-forth and the thirty-seventh weeks of gestation due to tubular blockage caused by Tamm-Horsfall protein precipitation, and may be a sign of hypoxic renal insufficiency (83). IUGR complicated with renal medullary hyperechogenicity suggests a more serious state, because these fetuses have a higher risk of pathological postnatal clinical outcome (83). IUGR not only leads to a low birth weight but is also hypothesized to reprogram nephrogenesis, which results in a low nephron endowment. According to the hyperfiltration hypothesis, this reduction in renal mass is supposed to lead to glomerular hyperfiltration and hypertension in remnant nephrons with subsequent glomerular injury with proteinuria, systemic hypertension and glomerulosclerosis in adult age (84).

5-1-2 Renal vein thrombosis

Renal vein thrombosis is the most common vascular condition in the newborn kidney and represents 0.5/1000 of admissions to neonatal intensive care units (85). Factors predisposing a neonate to renal vein thrombosis include dehydration, sepsis, birth asphyxia, maternal diabetes, polycythemia and the presence of indwelling umbilical venous catheter (85). In addition, prothrombotic abnormalities may be present in more than 40% of these babies and include Protein C or S deficiency, Factor V Leiden, Lupus anticoagulant and Antithrombin III deficiency (86). Renal vein thrombosis may also occur in utero; the origin of the thrombosis, however, is not always obvious. Sonographically, the fetal kidney appears somewhat enlarged; the cortex may appear hyperechoic and without corticomedullary differentiation. Pathognomonic vascular streaks may be visible in the interlobar areas. Thrombus in the inferior vena cava is a usual association (8). Color Doppler US may be used in addition to grey-scale examination in the assessment of renal vein thrombosis (Figure 3). After birth, the hyperechoic streaks and the thrombus are calcified. This feature helps differentiate antenatal from postnatal onset of the renal vein thrombosis (87).

5-1-3 The twin-to-twin transfusion syndrome

The twin-to-twin transfusion syndrome complicates 10 to 15% of monochorionic twin pregnancies (88). The etiology of this condition is not completely understood but is thought to result from an unbalanced fetal blood supply through the placental vascular shunts, with the larger twin being the recipient and the smaller twin the donor (89). The twin-to-twin transfusion syndrome is defined as presentation with the oligo-polihydramnios sequence (that is, the deepest vertical pool being 2 cm or less in the donor’s sac and 8 cm or more in the recipient's sac) (88). Additional phenotypic features in the donor include a small or nonvisible bladder and abnormal umbilical artery Doppler with absent or reverse end-diastolic frequencies. In addition to the neonatal complications of growth restriction, up to 30% of

donors have renal failure and/or renal tubular dysgenesis due to the chronic renal hypoperfusion state in utero (88). In the recipient, confirmatory features include large bladder, cardiac hypertrophy and eventually hydrops. Risk of renal failure in the recipient twin is considerably smaller than in the donor twin. This can be seen as one fetus dying and vascular resistance dropping significantly to cause reversed blood transfusion from the recipient twin to the dead fetus, resulting in hypovolemia and anemia in the live fetus (90).

5-1-4 Maternal drug intake

Some drugs taken by the mother can impair fetal renal function or produce congenital renal anomalies.

Angiotensin-converting enzyme Inhibitors: Angiotensin-converting enzyme Inhibitors (ACEIs) can severely affect renal development and function when used whatever the gestational age, and can lead to tubular dysgenesis, oligohydramnios, growth restriction, neonatal anuria and stillbirth (91, 92). The renal anomalies are thought to be caused first by a direct action of ACEIs on the fetal renin-Angiotensin system that reduces the concentration of angiotensin II, and then by secondary fetoplacental ischemia resulting from maternal hypotension and a drop of fetal-placental blood flow (60). Pregnancies exposed to ACEIs and complicated by an oligohydramnios present the highest rate of adverse pregnancy outcomes. In such cases, the combined use of amniotic fluid volume evaluation and fetal serum β2-microglobulin could help in the management of these pregnancies (93).

Angiotensin II receptor antagonists (ARBs): Many reports have described fetal abnormalities that are strikingly similar to those produced by maternal treatment with ACEIs, in association with maternal use of ARBs (94, 95). As for ACEIs, maternal treatment with ARBs should be avoided (95).

Nonsteroidal antiinflammatory drugs : Cyclooxygenase type 1 (COX-1) inhibitors such as indomethacin, the most common nonsteroidal antiinflammatory drug (NSAID) used

as a tocolytic, definitely reduce urine output and may lead to oligohydramnios and renal dysfunction (60). It was hoped that Cyclooxygenase type 2 (COX-2) inhibitors would target COX-2 activity and potentially spare COX-1-specific fetal side effects. However, human fetal kidneys have been shown to have an increase expression of COX-2 compared with adult kidneys, suggesting that COX-2 is constitutively expressed in the human fetal kidney (60). Experience with sulindac and nimesulide has therefore been linked with both constriction of the ductus arteriosus and oligohydramnios (96).

Cocaine: Maternal cocaine use adversely influences fetal renal function by hypoperfusion and thus influences the fetal renin-Angiotensin system. It is also associated with oligohydramnios as well as other fetal vascular complications leading to higher renal artery resistance index and a significant decrease in urine output (97). However, and contradicting a widely held belief (98), a prospective, large-scale, blinded, systematic evaluation for congenital anomalies in prenatally cocaine-exposed children did not identify any increase in the number or consistent pattern of genitourinary tract malformations (99).

Immunosuppressive medications during pregnancy: When the field of transplantation was first developing, physicians worried about the potential effects of immunosuppressive medications on the child-to-be and considered pregnancy ill-advised for patients taking these medications (100). Despite early concerns, a huge number of births among women with transplanted organs have been reported worldwide (101). Although some immunosuppressive drugs such as azathioprine, cyclosporine, have been found to be teratogenic in animals, registry records and case reports to date have found no unifying patterns of malformations in children of recipients of solid organs (102). However, data from offspring of women who took Mycophenolate mofetil (MMF) in pregnancy have increased concern that MMF may be teratogenic in humans (103). Therefore, European best practice guidelines recommend that

women receiving MMF transition to another agent and wait six weeks before they attempt to conceive (104).

5-2 Renal causes of congenital abnormalities of the kidney and urinary tract (CAKUT)

CAKUT are the most common cause of pediatric kidney failure. These disorders are highly heterogeneous, and the etiologic factors are not always understood. These disorders are genetically variable and encompass a wide range of anatomical defects, such as renal agenesis, renal hypodysplasia, pelviureteric junction stenosis, or VUR. Mutations in genes that cause syndromic disorders, such as *HNF1B* and *PAX2* mutations, are detected in only 5 to 10% of cases (105). Familial forms of nonsyndromic disease have been reported, further supporting genetic determination (such as *DSTYK* gene (106), *CHRM3* gene in Prune belly syndrome (107), *HPSE2* and *LRIG2* genes in Ochoa syndrome (108, 109)). However, owing to locus heterogeneity and small pedigree size, the genetic cause of most familial or sporadic cases remains unknown.

5-2-1 Multicystic dysplastic kidney (MCDK)

These kidneys contain bizarrely shaped tubules surrounded by a stroma that includes undifferentiated and metaplastic cells (for example, smooth muscle and cartilage). Data collected by Liebeschuetz (110) put the prevalence of MCDK at 1 in 2400 live births, which is higher than other reports (111). MCDK is usually unilateral and presents typical US pattern: multiple noncommunicating cysts of varying size and nonmedial location of the largest cyst, absence of normal renal sinus echoes, and absence of normal renal parenchyma (112). MCDK may also develop in the upper part of a duplex system or be located in an ectopic position. The prognosis for unilateral isolated MCDK is good, but meticulous

examination of the contralateral kidney is essential because there is a high incidence of associated pathologies, many of which may not be detected until birth (4, 113).

5-2-2 Autosomal recessive polycystic kidney disease (ARPKD)

ARPKD belongs to the family of cilia-related disorders and has an incidence of 1 in 20,000 live births and may cause fetal and neonatal death in severe cases. Mutations in the fibrocystin gene *PKHD1* are usually demonstrated in this disease (114). Yet, since some patients survive the neonatal period with few or slight symptoms, different combinations of mutations in *PKHD1* gene and its resulting changes in the fibrocystin/polyductin protein structure may at least partially explain the phenotypic variance (115). The disease is characterized by marked elongation of the collecting tubules that expand into multiple small cysts. The cystic dilatation of the tubules is variable and predominates in the medulla. The outer cortex is spared since it contains no tubules. The classical in utero pattern of ARPKD includes markedly enlarged (+4 SD) hyperechoic kidneys without corticomedullary differentiation. This appearance can be observed in the second trimester. The patterns may evolve and the size of the kidneys may continuously increase during the third trimester. Oligohydramnios and lung hypoplasia may be present, and therefore the prognosis is extremely poor. Another presentation of ARPKD is of reversed corticomedullary differentiation with large kidneys (+2 to +4 SD) (Figure 4). This finding is probably related to increased interfaces within the medullae and to the presence of material within the dilated tubules (116). It is an important observation since there are few other causes of reversed corticomedullary differentiation. The liver involvement typical of the condition is usually impossible to demonstrate in utero. The differential diagnosis includes the glomerulocystic type of autosomal dominant polycystic kidney disease, Bardet-Biedl syndrome in which polydactyly is present (46) and other rare entities such as bilateral renal tumors, medullary sponge kidney, bilateral nephroblastomatosis, congenital nephrotic syndrome of the Finnish

type, medullary cystic disease, or congenital metabolic diseases (that is, glycogen storage disease or tyrosinosis). Oligohydramnios and absence of urine within the bladder would favor ARPKD over all of these rare entities.

5-2-3 Autosomal dominant polycystic kidney disease (ADPKD)

ADPKD is a common hereditary kidney disease, with 1/1000 people carrying the gene. The pathological abnormality consists of cystic dilatation of all parts of the nephron, which causes the kidneys to enlarge as the cortex and medulla become replaced by cysts, thus leading to end-stage renal failure (116, 117).

There are two major types of ADPKD: type I is caused by mutations in the *PKD1* gene on chromosome 16p13.3 and accounts for 85% to 90% of cases (116), and type II is caused by mutations in the *PKD2* gene on chromosome 4q21-22 and accounts for 10% to 15% of cases (117). One or more other genes (type III) are likely involved since some obvious cases have none of these mutations. Although the age of clinical onset of this disorder is typically in the third to fifth decade of life, early manifestations during childhood or during the prenatal period have been reported (118, 119).

There may be two different presentations in utero. In most cases, the kidneys are not grossly enlarged, but the corticomedullary differentiation is increased due to cortical hyperechogenicity. In this type of ADPKD, cysts are unusual in utero; they will develop after birth. Markedly enlarged kidneys resembling ARPKD are another pattern that can be encountered in utero and suggests the glomerulocystic type of ADPKD. In this presentation of the disease, some subcortical cysts may be present in utero and renal failure may appear at birth (115).

5-2-4 Renal hypoplasia and dysplasia

Renal dysplasia refers to abnormal differentiation or organization of cells in the renal parenchyma and is characterized histologically by the presence of primitive ducts and nests of metaplastic cartilage (23, 24). Hypoplasia is a reduction of the number of nephrons in small kidneys (below -2 SD) (23). Hypoplasia may coexist with dysplasia and the diagnosis is inferred from the hyperechoic appearance on US caused by the lack of normal renal parenchyma and structurally abnormal small kidneys (23, 24) (Figure 5). As in most cases the diagnosis is made by US examination, the spectrum of renal dysplasia includes inherited or congenital causes of renal hypoplasia, renal adysplasia, cystic dysplasia, oligomeganephronic hypoplasia, reflux nephropathy and obstructive renal dysplasia (23). Cases with oligohydramnios have the poorest outcome (120).

A number of developmental genes, such as *EYA1* and *SIX1* causing autosomal dominant branchio-oto-renal syndrome (121), *HNF1B/TCF2* associated with autosomal dominant renal cysts and diabetes syndrome (122), and *PAX2* causing autosomal dominant renal-coloboma syndrome (123), have been implicated in the pathogenesis of hypodysplastic kidneys (105).

After birth, the prognosis depends on the remaining renal function at 6 months of age. Infants with a GFR below 15 ml/min per 1.73 m² are at higher risk for early renal replacement therapy (23).

5-2-5 Congenital nephrotic syndrome

Congenital nephrotic syndrome is defined as proteinuria leading to clinical symptoms during the 3 months after birth. Infantile nephrotic syndrome manifests later, in the first year of life. These classifications, however, are arbitrary because the majority of early-onset nephrotic syndrome diseases range from fetal life to several years of age (124).

Congenital nephrotic syndrome of the Finnish type (CNF) is characterized by

autosomal recessive inheritance and is caused by mutations in the nephrin gene (*NPHS1*) (125). The incidence is 1 of 8200 births in Finland, but it occurs worldwide. Most infants are born prematurely, with low birth weight for gestational age. The placenta is enlarged, weighing more than 25% of the birth weight. Edema is present at birth or appears within a few days due to severe nephrotic syndrome. In utero, the possible development of Hydrops fetalis and increased nuchal translucency reflects massive proteinuria paralleled by a relatively high urine output (126, 127). Because the main part of amniotic fluid α-fetoprotein is derived from fetal urine, high values reflect intrauterine proteinuria (128). If the α-fetoprotein concentration is 250,000 to 500,000 μg/l, and especially if there is another child with CNF in the family, it is highly suggestive of CNF.

Podocin gene (*NPHS2*) mutations have also been reported in patients with congenital nephrotic syndrome (129). However, the severity of the disease is variable and may occur at birth, in childhood or later in adulthood (124). Patients with podocin mutants that are retained in the endoplasmic reticulum, such as the R138Q mutant, are associated with the earliest onset of the disease (129).

Pierson syndrome is a rare, lethal, autosomal recessive entity that includes congenital nephrotic syndrome attributable to diffuse mesangial sclerosis, in association with distinct eye abnormalities clinically characterized by bilateral microcoria (130). The defective gene (*LAMB2*) has been localized to chromosome 3p21 and leads to a lack of laminin β2, an important constituent of the glomerular and other basement membranes (131). In utero, fetuses may present, as in CNF, hydrops fetalis and increased nuchal translucency. However, these findings are inconstant because severe renal failure may be already present in these fetuses, leading to early regression of urine output, oligohydramnios and sometimes consecutive pulmonary hypoplasia (130). Fetal kidneys appear impressively more hyperechoic than those reported in fetuses with CNF (132).

Other cases of prenatally diagnosed congenital nephrotic syndrome have been reported including isolated, sporadic or familial diffuse mesangial sclerosis (124, 133), secondary nephrotic syndrome due to CMV or other intrauterine infections (134) and massive proteinuria in offsprings of mothers with homozygous deficiency for the metallomembrane endopeptidase (71).

5-3 Postrenal Causes of Fetal Renal Abnormalities

Dilatations of the renal pelvis, calyces and ureters are the principal signs of impaired urinary flow on antenatal ultrasound scanning.

5-3-1 Pelviureteric junction stenosis

Pelviureteric junction stenosis occurs in 13% of children with antenatally diagnosed renal pelvis dilatation (29) and is characterized by obstruction at the level of the junction between the renal pelvis and the ureter. The anatomical basis for obstruction includes intrinsic stenosis/valves, peripelvic fibrosis, or crossing vessels. Sonographic diagnosis depends on the demonstration of a dilated renal pelvis in the absence of any dilatation of ureter or bladder. It should be particularly suspected when moderate (10 to 15 mm) or severe (greater than 15 mm) dilatation is seen, when the cavities appear round shaped and in the presence of a perirenal urinoma (26) (Figure 6). Prognosis may be poor in bilateral cases associated with oligohydramnios and hyperechoic parenchyma. Postnatal management of these children still remains a controversial topic among the nephro-urologic community (131). Expectancy and close follow-up (135, 136) have progressively gained wide acceptance, although the surgical attitude, either systematic within the first months of life, or on the basis of variable morphological or functional parameters, is still the present attitude for many clinicians (137). However, the final outcome, being when these children have reached old age, is remote.

5-3-2 Vesicoureteric reflux (VUR)

VUR is defined as the retrograde flow of urine from the bladder upward within the ureter, sometimes extending into the renal pelvis, calyces and collecting ducts. Fetal renal pelvis dilatation can signal the presence of VUR in 11% (29) to 30% (138) of cases with the lower figure being more realistic. Making a precise diagnosis of VUR in utero is difficult. However, intermittent renal collecting system dilatation during real-time scanning (Figure 7) or pelvicaliceal wall thickening are good sonographic criteria supporting the diagnosis (139). The arguments surrounding the importance of diagnosing all cases of neonatal VUR center on the perceived magnitude of the risks of infection and functional decline. However, current evidence suggests that only patients with grades IV to V disease are at high risk of serious adverse outcome and delayed resolution (140). Although some children with prenatal VUR may have already renal lesions, namely congenital dysplasia due to high-grade disease, VUR related to fetal renal pelvis dilatation was found in a large and prospective study to be of low-grade in 74% of cases with a high rate of 2-year spontaneous resolution (91%) (6). Therefore, it is unclear whether low-grade reflux detected antenatally is necessarily clinically significant. It is also unclear whether asymptomatic antenatally detected VUR and symptomatic postnatal VUR are the same pathologies (26).

5-3-3 Uretero-vesical junction obstruction (Megaureter)

In utero, under normal conditions, the ureters are not visualized. Megaureter should be suspected in the presence of a serpentine fluid-filled structure with or without dilatation of the renal pelvis and calices (Figure 8). The ureter may be dilated because of obstruction at the level of the junction between the ureter and the bladder or as a result of nonobstructive causes including high-grade reflux. The differential diagnosis relies on VCUG. Megaureter could also be encountered in fetuses and /or newborns with neurogenic bladder or posterior urethral valves. In those cases, specific treatment strategies should be directed toward the underlying

condition. Prognosis of primary megaureter is generally good since most cases resolve spontaneously between ages 12 and 36 months (141). However, in children with high-grade hydronephrosis, or a retrovesical ureteral diameter of greater than 1 cm, the condition may resolve slowly and may require surgery (141).

5-3-4 Duplex kidneys

Duplication of the renal collecting system is characterized by the presence of a kidney having two pelvic structures with two ureters that may be completely or partially separated (142). Most cases with nondilated cavities have no renal impairment and should be considered as normal variants (29). However, a proportion of duplex kidneys may be associated with significant pathology, usually due to the presence of VUR or obstruction. Fetal urinary tract dilatations are related to complicated renal duplication in 4.7% of cases (29). VUR usually involves only the lower pole ureter in 90% of cases. Compared to single-system reflux, duplex system VUR tends to be of a higher grade with a high incidence of lower pole dysplasia (5, 143). Obstructive ureteroceles are associated with the upper pole ureter in 80% of cases, although obstruction of the upper pole may also occur secondary to an ectopic insertion or an isolated vesicoureteric junction obstruction (142). In utero, duplex kidneys are highly suspected in the presence of two separate noncommunicating renal pelves, dilated ureters, cystic structures within one pole, and echogenic cyst in the bladder, representing ureterocele (144). After birth, the classical radiological workup of abnormal duplex kidneys is based on US and VCUG (145). The aim of US is to confirm the diagnosis, whereas VCUG is performed in order to detect VUR and to evaluate the ureterocele. In complex cases, with significant dilatation, the diagnosis may be clarified by fetal MR imaging (3). Isotope studies are mandatory to determine renal function that remains in the dilated renal moiety. Most people agree that the surgical approach to complicated duplex systems is largely predicated on the function of the affected renal moiety and the presence or absence of function (145).

Regardless of the nature of the diseased moiety, however, the evolution of the functioning moiety seems favorable over time with remarkable stable split renal function around 40% (5).

5-3-5 Bladder outlet obstruction

When bladder obstruction is suspected in the first trimester, the most common causes are Prune Belly syndrome or fibrourethral stenosis, which is mainly associated with chromosomal and multiple congenital anomalies and carries a very poor prognosis (146). In the second trimester, the most common cause of lower urinary tract obstruction in male fetuses is posterior urethral valves, which are tissue leaflets fanning distally from the prostatic urethra to the external urinary sphincter. The failure of the bladder to empty during an extended examination and the presence of abnormal kidneys and oligohydramnios must raise suspicion of posterior urethral valves. On occasion a megabladder with a thickened wall may be seen, and the dilated posterior urethra may take the aspect of a keyhole (Figure 9). In extreme cases in utero bladder rupture may be observed with extravasation of urine resulting in urinary ascites. This phenomenon was thought to be a protective pop-off mechanism, although recent reports provided evidence against this hypothesis (147).

In many cases there is only a partial obstruction, and amniotic fluid volume can be maintained throughout pregnancy. In some cases, spontaneous rupture of valves appears to occur in utero with the reappearance of cyclical emptying of the bladder. The most reliable prognostic indicators of poor renal functional status are presentation before 24 weeks, oligohydramnios, increased cortical echogenicity, and the absence of corticomedullary differentiation (148)

The prognosis in severe cases is often relatively easy to predict, and perinatal death will occur secondary to pulmonary hypoplasia and renal failure (149). The renal parenchymal lesions may be secondary to the obstruction but also to associated high-grade reflux. In partial obstruction, however, the outcome is less predictable, and late morbidity most commonly takes the form of end-stage renal failure, which affects 15 to 30% of individuals some time in

childhood (150). Once the prognosis has been determined as accurately as possible, management of these cases should be performed in a fetal medicine and pediatric surgery reference center. In each new case, the great variability of presentation makes participation of different specialists necessary in the difficult decision-making process. Various options should be discussed, including in utero follow-up with planned postnatal management, termination of pregnancy, and occasionally, in utero therapy.

It may appear reasonable to imagine that an antenatal intervention to relieve the obstruction after diagnosis may restore amniotic fluid levels, thereby allowing normal pulmonary maturation. Whether early intervention may prevent progressive renal deterioration or improve long-term renal outcomes, however, remains to be determined. A variety of in utero therapeutic approaches to bladder outflow obstruction have been tried. The open surgical technique of fetal vesicostomy has been abandoned due to significant fetal loss, premature uterine contractions and maternal morbidity (151). Vesicoamniotic shunting is performed with US guidance using a pigtail shunt, which when inserted leaves one end in the fetal bladder and the other in the amniotic space. The morbidity of this technique is high with a perinatal mortality of 53% and shunt complications of 45% (74). Furthermore, end-stage renal failure was present in 40% of those children who survived (74). Direct endoscopic ablation of the valves is a more recent technique and requires the introduction of an endoscope into the fetal bladder, leading to ablation of the valves either by laser, saline irrigation or mechanical disruption using guide wire (152, 153). Direct visualization of the valves, however, is difficult, and it may be hard to avoid damage to surrounding tissues. Unfortunately, experience with these techniques did not support any advantage in terms of postnatal bladder dynamics or renal function improvement (154).

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	Kidney size	Amniotic fluid volume	Renal cysts	Collecting system	Associated abnormalities	Inheritance	Alternative prenatal diagnosis
Obstruction	-2 to 0 SD	Normal or reduced	Cortical < 1 cm	Dilated	No	Sporadic	MRI
Bilateral MCDK	Variable	Reduced	Variable sizes, mostly large	Not seen	Variable if syndromic	Sporadic	MRI
Renal vein thrombosis	0 to 2 SD	Normal	No	Not seen	Thrombus in the inferior vena cava	Sporadic	Doppler
ARPKD	2 to 4 SD	Reduced	Small medullary	Not seen	Lung hypoplasia	AR	Genetics
ADPKD	0 to 2 SD	Normal or reduced	Subcapsular and medullar	Not seen	No	AD	Genetics
Glomerulocystic dysplasia	0 to 2 SD	Variable	Small cortical	Not seen	Variable if syndromic	Variable	Genetics (*HNF1B/TCF2*)
Bardet-Biedl syndrome	2 to 4 SD	Variable	No or medullary	Not seen	Polydactyly	AR	Genetics
Beckwith-Wiedeman syndrome	2 SD	Normal or increased	No or medullary	±	Macrosome, omphalocele	AD or dysomy	Genetics
Perlman syndrome	2 SD	Normal or reduced	No	±	Macrosome	AR	-
Normal variant	0 to 2 SD	Normal or increased	No	±	No	Sporadic	-

Table 1: Conditions associated with hyperechoic kidneys.

ARPKD, Autosomal recessive polycystic kidney disease; ADPKD, Autosomal dominant polycystic kidney disease; MCDK, Multicystic dysplastic kidney; AD, Autosomal dominant; AR, Autosomal recessive; MRI, Magnetic resonance imaging; HNF-1β, Hepatocyte nuclear factor-1β.

Authors	Year	Threshold value of renal pelvis (mm)	Total	Abnormal (%)	UPJS (%)	VUR (%)	Megaureter (%)	Mild dilatation (%)	Duplex kidney (%)	Other (%)	(%) undergoing surgery
Dudley et al. (32)	1997	5	100	64	3	12	3	43	4	7	3
Stocks et al. (33)	1996	4-7	27	70	22	22		26			11
Jaswon et al. (34)	1999	5	104	45	4	22		8		4	1
Ismaili et al. (29)	2004	4-7	213	39	13	11	7	18*	5	3	3

Table 2: Incidence of uro-nephropathies in neonates with antenatally diagnosed renal pelvis dilatation. UPJS (uretero-pelvic junction stenosis), VUR (vesicoureteral reflux).

*In this study mild and transient dilatations were considered as non significant findings.

	Renal cysts	Associated abnormalities	Inheritance	Reference
Meckel-Gruber syndrome	Medullary	Encephalocele, brain/cardiac anomalies, hepatic ductal dysplasia, cleft lip/palate, polydactyly	AR	(44)
Trisomy 9	Medullary	Mental retardation, intrauterine growth retardation, cardiac anomalies, joint contractures, prominent nose, sloping forehead	Chromosomal	(45)
Trisomy 13	Medullary	Mental retardation, intrauterine growth retardation, cardiac anomalies, cleft lip/palate, polydactyly	Chromosomal	(45)
Trisomy 18	Medullary	Mental retardation, intrauterine growth retardation, cardiac anomalies, small face, micrognathia, overlapping digits	Chromosomal	(45)
Bardet-Biedl syndrome	No or medullary	Polysyndactyly, obesity, mental retardation, pigmented retinopathy, hypogonadism	AR	(46)
Zellweger syndrome	Medullary	Hypotonia, seizures, failure to thrive, distinctive face, hepatosplenomegaly	AR	(47)
Ivemark syndrome	No or medullary	Polysplenia, complex heart disease, midline anomalies, situs inversus	Sporadic, AR	(48)
Beckwith-Wiedeman syndrome	Medullary	Overgrowth, macroglossia, omphalocele, hepatoblastoma, Wilm's tumor	Sporadic, AD	(49)
Jeune's syndrome	Medullary	Narrow chest, short limbs, polydactyly, periglomerular fibrosis	AR	(50)
Tuberous sclerosis	Medullary	Mental retardation, seizures, facial angiofibroma, angiomyolipoma, hypopigmented spots, cardiac rhabdomyomas, cerebral hamartomas	AD	(51)

Table 3: Syndromes with cystic renal disease.

AD, Autosomal dominant; AR, Autosomal recessive.

	Origin	Pathologies
Oligohydramnios	Uronephropathy	Bilateral renal agenesis
		Bilateral renal dysplasia
		Autosomal recessive polycystic kidney disease
		Bilateral obstructive uropathy
		Bilateral high-grade reflux
		Bladder outlet obstruction
	Other	Premature rupture of membranes
		Placental insufficiency
		fetal death
		Fetal growth retardation
		Twin-to-twin transfusion (twin donor)
		Maternal drug intake: prostaglandin synthase inhibitors, angiotensin-converting enzyme inhibitors, cocaine
		Postmaturity syndrome
Polyhydramnios	Uronephropathy	Renal tumors, especially mesoblastic nephroma
		Bartter syndrome
		Congenital nephrotic syndrome
		Alloimmune glomerulonephritis
	Other	Maternal diabetes
		Maternal drug intake: lithium,
		Multiple gestations
		Twin-to-twin transfusion (twin recipient)
		Fetal infections: Rubella, Cytomegalovirus, Toxoplasmosis
		Fetal gastrointestinal obstructions: esophageal atresia, duodenal atresia, gastroschisis
		Fetal compressive pulmonary disorders: diaphragmatic hernia, pleural effusions, cystic adenomatoid malformations, narrow thoracic cage
		Neuro-muscular conditions: anencephaly, myotonic dystrophy
		Cardiac anomalies
		Hematologic anomalies (fetal anemia)
		Hydrops fetalis
		Fetal chromosome abnormalities: trisomy 21, trisomy 18, trisomy 13
		Syndromic conditions: Beckwith-Wiedeman syndrome, achondroplasia
		No evident cause

Table 4: Causes of oligohydramnios and polyhydramnios.

	Normal limits (74)	Good prognosis (75, 76)	Post natal moderate renal failure after 1 year (77)	Poor prognosis (Neonatal death or termination of pregnancy) (76, 77)
Na+	75-100 mmol/l	< 100 mmol/l	59 mmol/l (54-65)	121 mmol/l (100-140)
Ca++	2 mmol/l		2 mmol/l (1.5-2.5)	2 mmol/l (1.5-2.5)
Cl^-		< 90 mmol/l	57 mmol/l (52-62)	98 mmol/l (85-111)
β2-microglobulin	< 4 mg/l	< 6 mg/l	6.77 mg/l (4.16-9.37)	19.5 mg/l (11-28)
Cystatin C		< 1 mg/l	0.47 mg/l (0.05-4.75)	4.1 mg/l (0.45-13.1)
Osmolarity	< 200 mOsm/l	< 210 mOsm/l		

Table 5: Fetal urine biochemical markers by groups of outcome.

	α1-microglobulin (mg/L)	β2-microglobulin (mg/L)	Cystatin C (mg/L)
Uropathies			
Termination of pregnancy	67.9 (22.0–150)	7.4 (5–12.5)	2 (0.83–3.35)
Neonatal death	60.3 (35.4–119)	7.6 (6.4–9.2)	2.12 (1.62–3.77)
Postnatal renal failure	60.5 (31.8–90.1)	5.3 (3.5–7.2)	1.95 (1.56–4.60)
Postnatal normal renal function	34.4 (20.4–100)	3.9 (1.8–5.4)	1.67 (1.05–2.26)
Nephropathies			
Termination of pregnancy	93.4 (21.2–140.4)	8.1 (2.8–13.6)	2.23 (1.45–3.53)
Neonatal death	53.8 (18.1–73)	8.9 (5.7–10.4)	2.48 (1.54–2.60)
Postnatal renal failure	46.0 (18.3–82.8)	5.6 (2.6–13.9)	2.22 (1.48–4.39)
Postnatal normal renal function	27.5 (23.3–52.5)	2.8 (2.6–6.4)	1.70 (1.42–2.77)

Table 6: Median values of fetal serum biochemical markers by groups of outcome, according to Nguyen et al. (81).

Legend to figures:

Figure 1: Normal fetal kidney (third trimester). Sagittal scan of the kidney (k). Corticomedullary differentiation is clearly visible (arrowheads).

Figure 2: Algorithm of a rational postnatal imaging strategy in infants with mild to moderate fetal renal pelvis dilatation.

Figure 3: Left renal vein thrombosis (third trimester). A. Axial US scan showing differences of size and echogenicity of both kidneys, The left kidney is enlarged and hyperechoic. B. Coronal US scan showing normal renal venous flow on the right kidney. C. Parasagittal US scan of the left kidney. Renal venous flow is almost absent in comparison with the normal right kidney

Figure 4: Autosomal recessive polycystic kidney disease. Third trimester-coronal scan through the kidneys that appear large (+3 SD), and hyperechoic.

Figure 5: Renal hypodysplasia (third trimester). Sagittal US scan through a hyperechoic right kidney. A medullar cyst is present (between crosses). L: liver.

Figure 6: Pelvicaliceal dilatation and perirenal urinoma (arrow) in a fetus with pelviureteric junction stenosis. Coronal US scan through the right fetal kidney.

Figure 7: Fetal vesicoureteral reflux. Transverse scans of the fetal abdomen. Intermittent renal collecting system dilatation during the same antenatal ultrasound examination due to vesicoureteral reflux.

Figure 8: Megaureter. In utero (third trimester) dilatation of the right ureter. Transverse scan of the fetal abdomen showing a serpentine fluid-filled structure. The ureter measures 9 mm (between the crosses).

Figure 9: Megabladder. Third trimester. Huge enlargement of the fetal bladder due to posterior urethral valves. The key-hole sign is present.

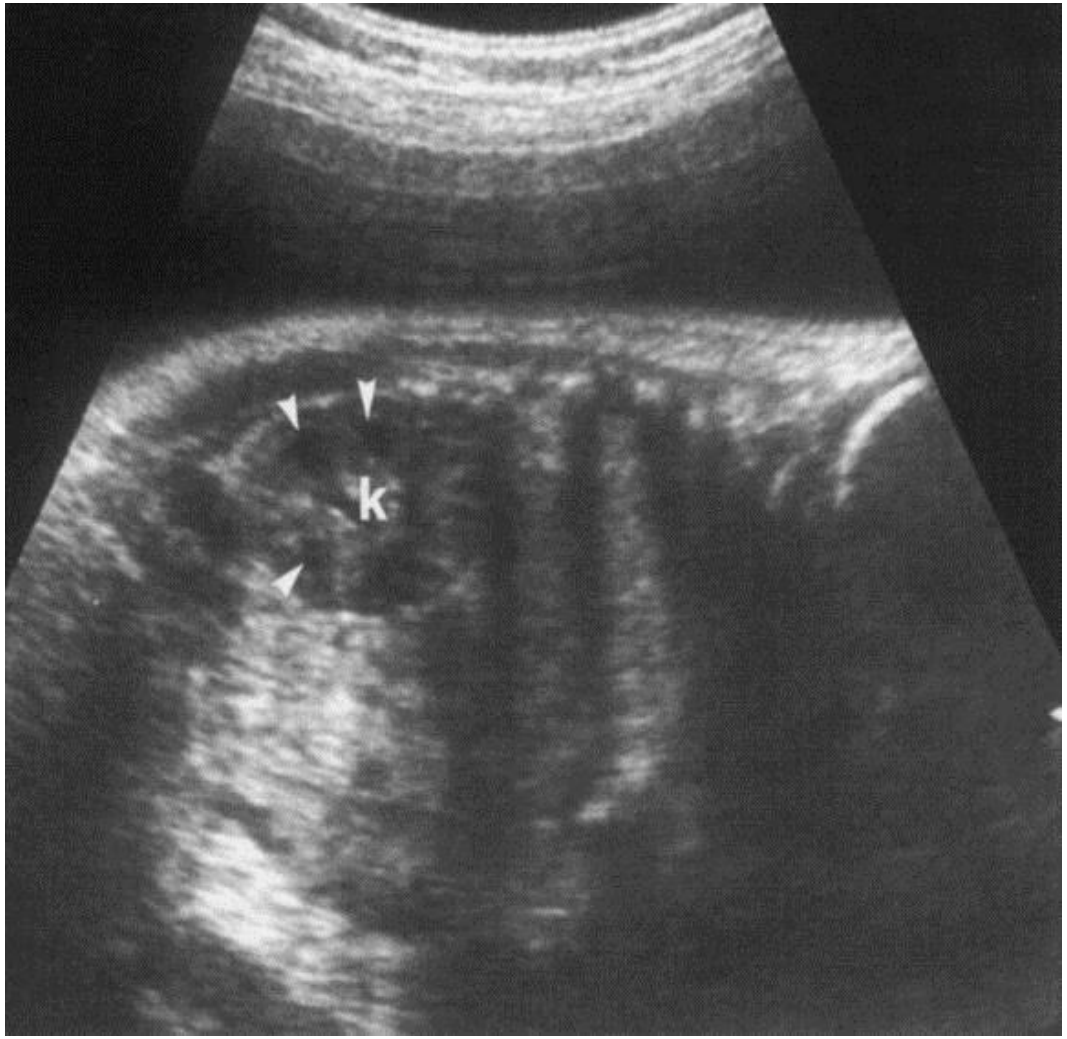

Fig 1

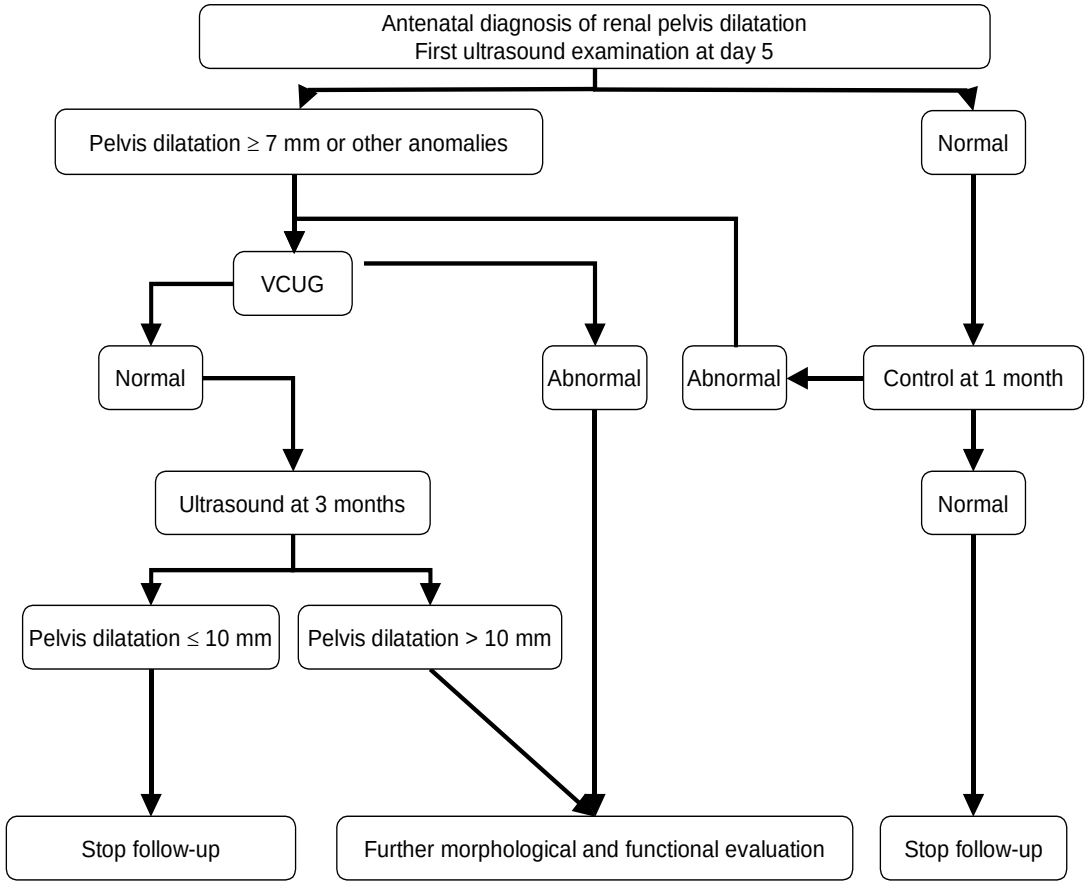
Antenatal diagnosis of renal pelvis dilatation
First ultrasound examination at day 5
Pelvis dilatation ≥ 7 mm or other anomalies
Normal
VCUG
Normal
Abnormal
Abnormal
Control at 1 month
Ultrasound at 3 months
Normal
Pelvis dilatation ≤ 10 mm
Pelvis dilatation > 10 mm
Stop follow-up
Further morphological and functional evaluation
Stop follow-up

Fig 2

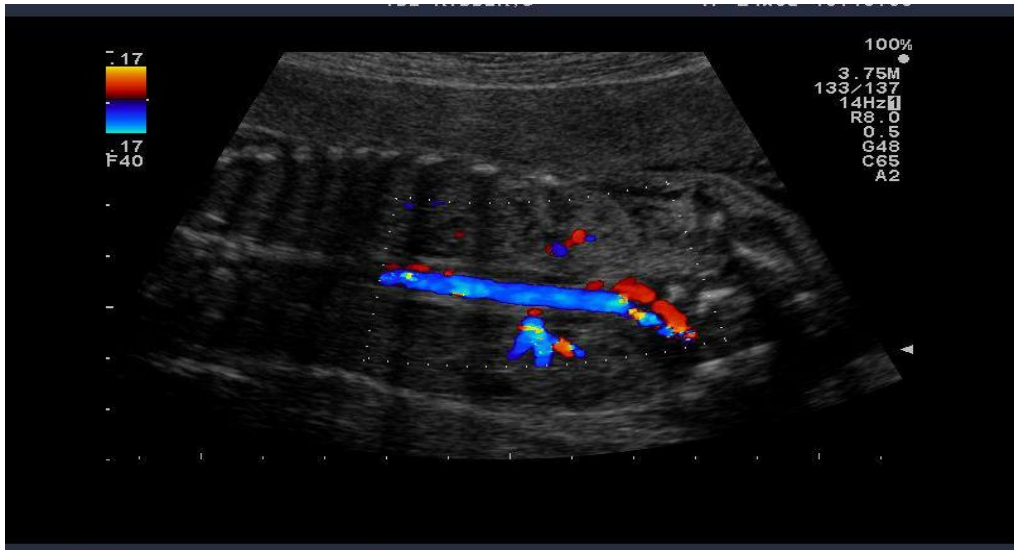

Fig 3

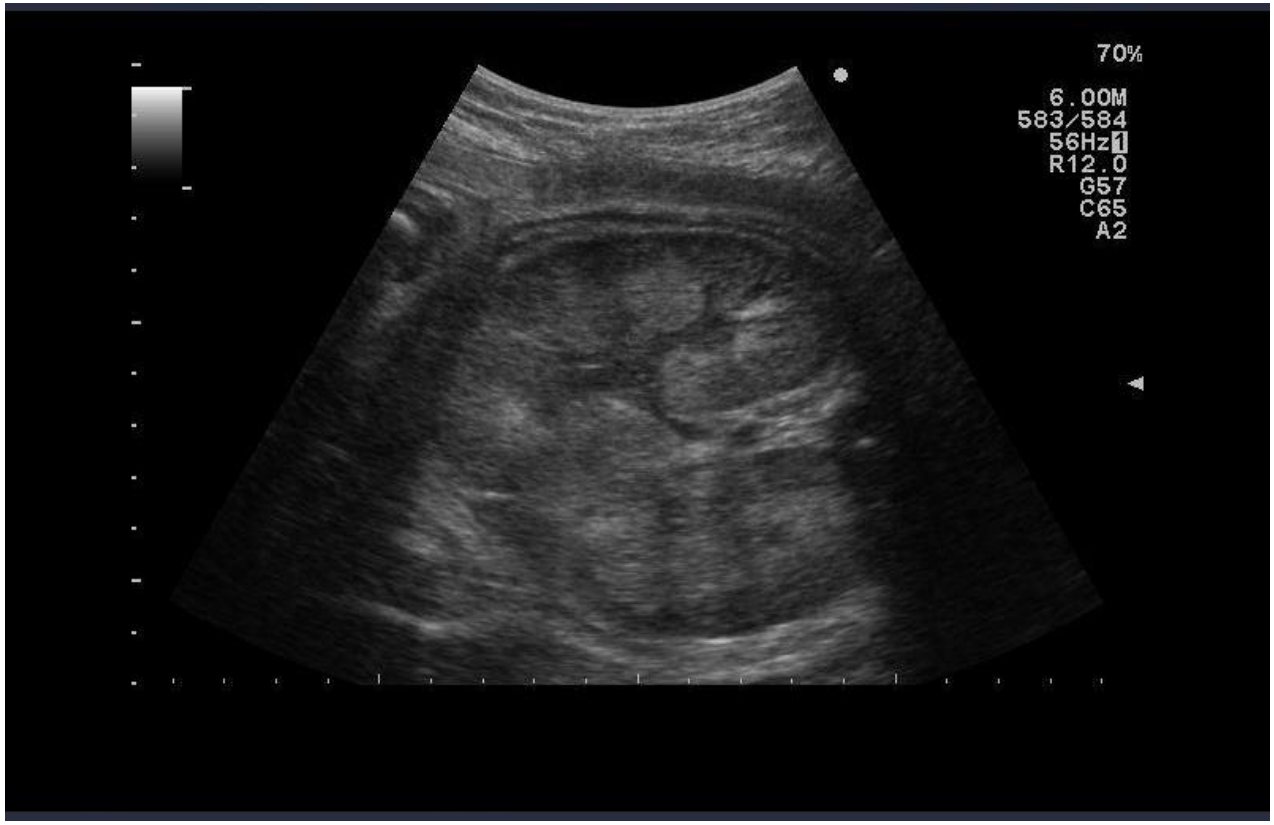

Fig 4

Fig 5

Fig 6

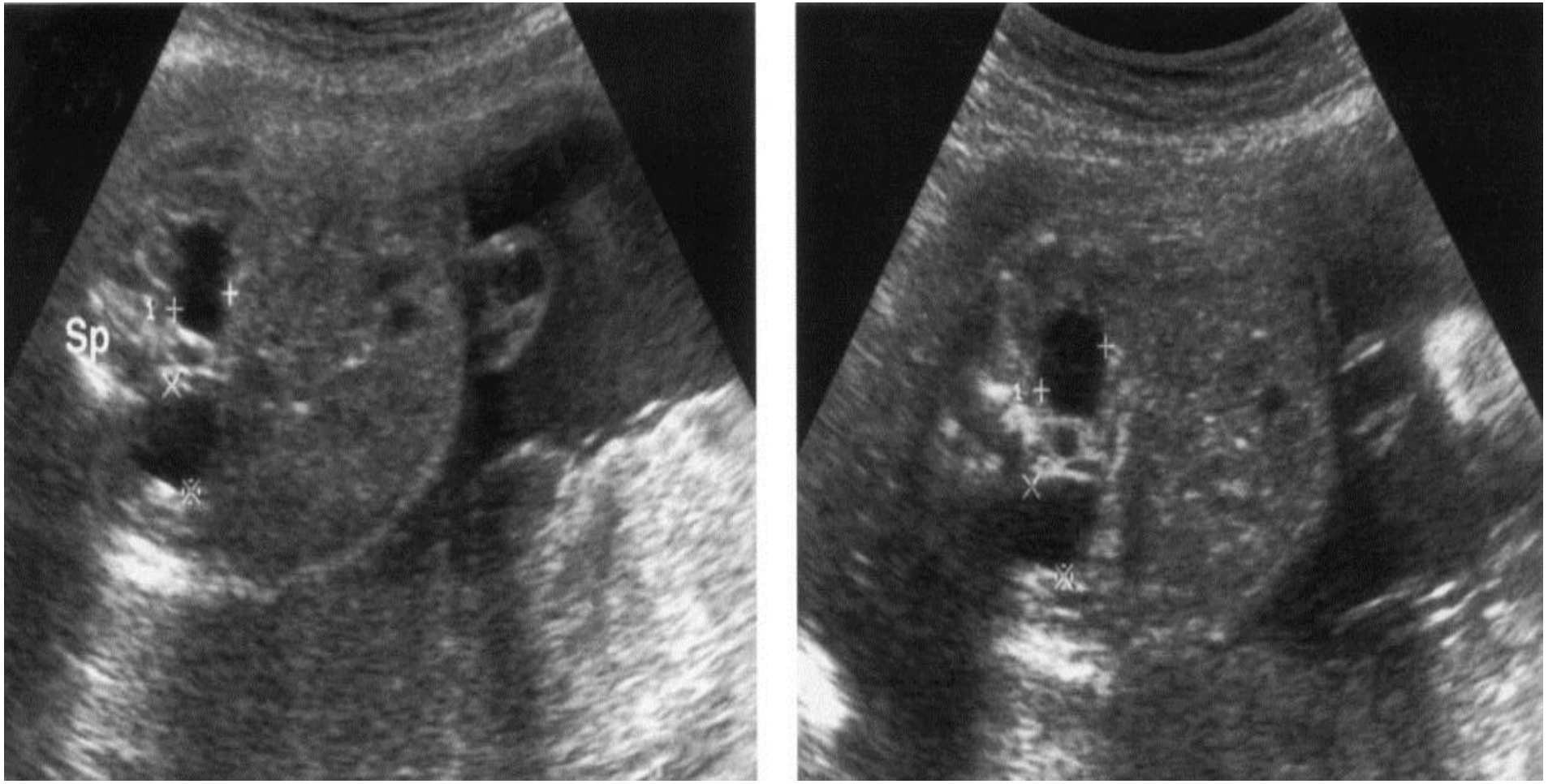

Fig 7

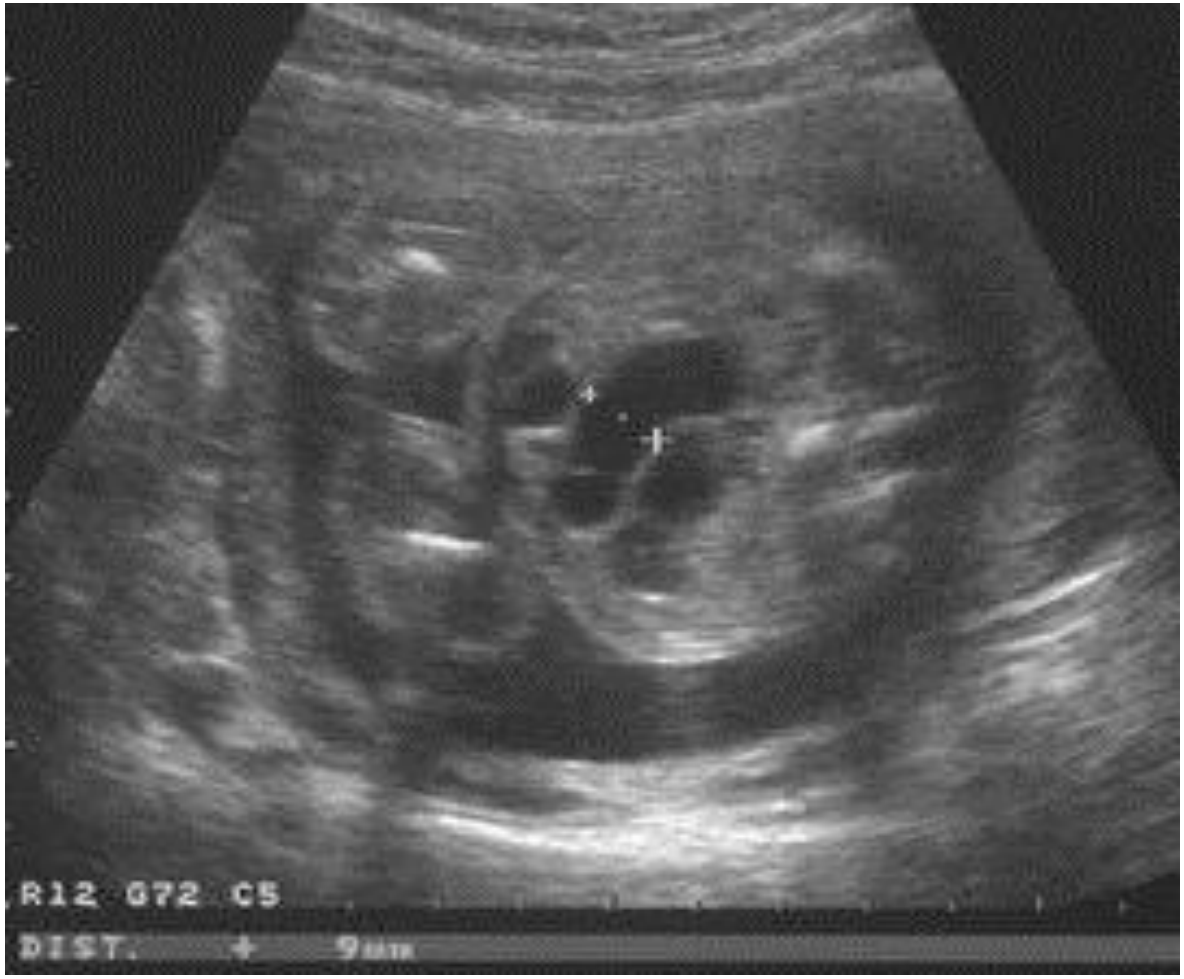

Fig 8

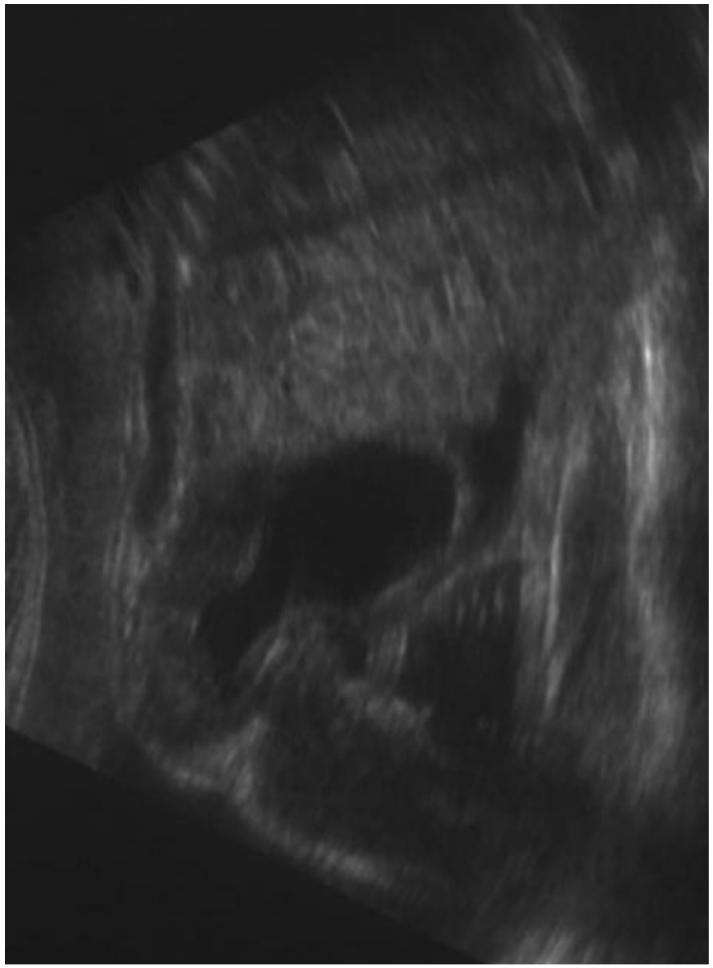

Fig 9