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REVIEW ARTICLE

Practical Management of Fetal Obstructive Uropathy

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Abstract Urinary tract dilatation is commonly identified on antenatal ultrasound. It represents a wide range of aetiologies including obstructive uropathy. Antenatal diagnosis and a consistent, evidenced based approach to follow up is essential in reducing neonatal morbidity and mortality. We present a summary of the current literature and a practical guide to the management of obstructive uropathy, including the normal sonographic features of the developing fetal urinary tract, antenatal diagnostic criteria and the approach to postnatal investigation and management.

Keywords Obstructive uropathy · Hydronephrosis · Antenatal · Postnatal · Ultrasonography

Introduction

Dilatation of the urinary tract is the most common anomaly detected by antenatal ultrasound, present in 1% of pregnancies [1]. It represents a wide range of different aetiologies, including the possibility of obstructive uropathy.

Antenatal diagnosis of obstructive uropathy is important as it allows for surveillance and early neonatal treatment, preventing the progression of worsening renal disease. This review article describes the current antenatal and postnatal approach to the investigation, diagnosis and management of obstructive uropathy.

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Normal Ultrasound Features of the Urinary Tract

The ultrasound examination of the fetal urinary tract should follow a structured approach. It includes identification of the presence, location and size of the fetal kidneys, as well as examination of the urinary bladder, genitalia and an assessment of amniotic fluid volume.

The fetal kidneys are first seen sonographically from approximately 12–14 weeks' gestation in the paravertebral region [2]. They initially appear uniformly hyperechoic, until cortico-medullary differentiation occurs between 15 and 24 weeks', when the renal cortex can be easily distinguished from the medulla [3] (Fig. 1).

Measurements of the external renal structure should be taken in the longitudinal, anteroposterior (AP) and transverse planes, allowing for the calculation of the renal volume. The measurements increase proportionally with gestation as per established centile norms [4].

An assessment of the renal pelvis should be made by measuring the AP renal pelvis diameter (APRPD), achieved in the transverse plane at its maximal diameter (Figs. 2, 3). It is important to observe for any calyceal dilatation, parenchymal changes, or anomalies of the collecting system (e.g. duplex). In the normal fetus, the ureters are not usually seen and their presence on ultrasound should alert to an underlying pathology.

The fetal bladder is observed from 11 weeks, appearing as an anechoic structure within the pelvis between the 2 vitelline arteries [2]. Assessment of the bladder should include its position, size and wall thickness. Enlargement of the bladder, failure of the bladder to empty over

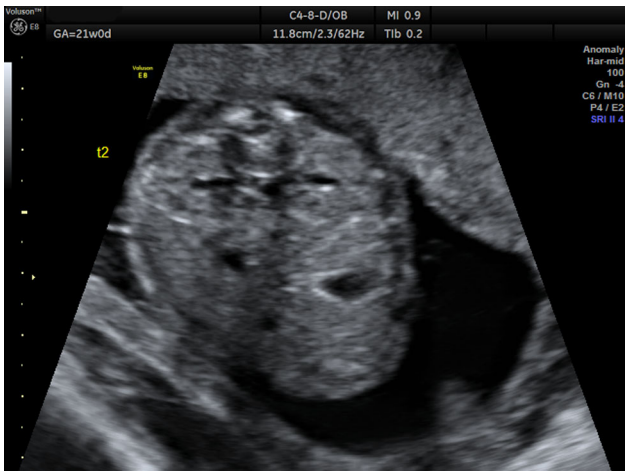

Fig. 1 Normal fetal kidney in the 2nd trimester—fetal kidneys in the transverse plane, demonstrating paravertebral location in abdomen and clear cortico-medullary differentiation. Convention is that they imaged in the spine-up position

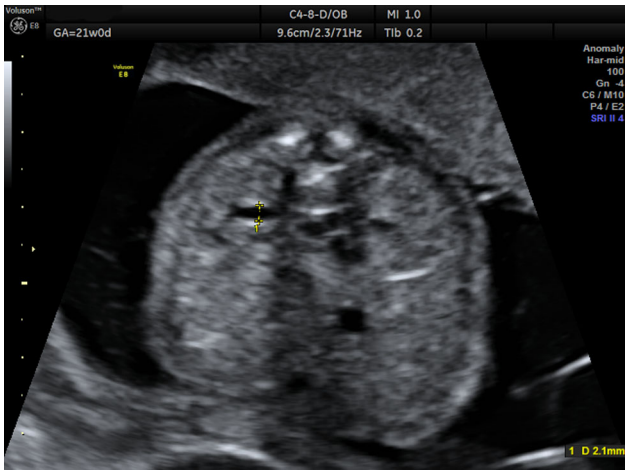

Fig. 2 Estimation of APRPD—the renal pelvis is demonstrated medially and appears as an anechoic structure. The anteroposterior renal pelvis diameter (APRPD) is measured at its maximal diameter, here measuring 2.1 mm on the right kidney

30–45 min and thickening of the bladder wall are indicative of outflow obstruction [5].

Amniotic fluid is assessed objectively by calculating the amniotic fluid index (AFI) or deepest vertical pool (DVP). In normal pregnancy, liquor volume increases until around 30 weeks', before gradually declining towards term [6].

Antenatal Diagnosis of Obstructive Uropathy

There is a lack of consensus around the classification and nomenclature when describing urinary tract dilatation (UTD). Pyelectasis, hydronephrosis, pelviectasis, uronephrosis, urinary tract prominence and pelvic fullness

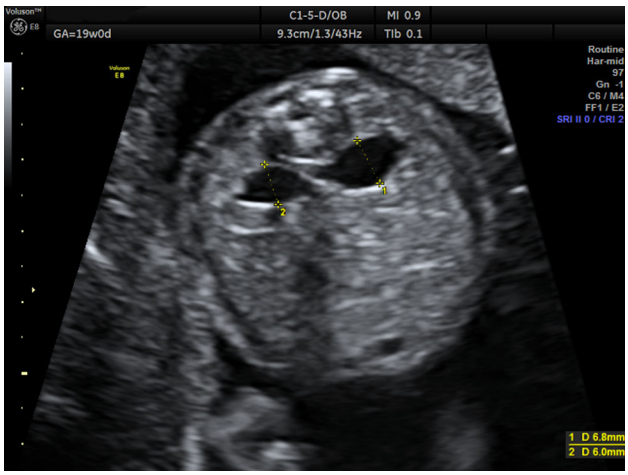

Fig. 3 Urinary tract dilation—bilateral measurements of APRPD. The right kidney measures 6.0 mm and the left kidney 6.8 mm. In the UK, the NHS Fetal Anomaly Screening Programme guidelines classify this as normal and no further investigation and follow-up would be required. Other authors, who use a more stringent cut-off for APRPD would advise a follow-up ultrasound in the third trimester

are all commonly used descriptions and often used incorrectly and synonymously. To avoid ambiguity, Nguyen et al. have suggested the term UTD which encompasses all dilatation of the urinary tract, including the above diagnoses [7].

The APRPD is the most commonly accepted measurement for the diagnosis of UTD, although there is no universally accepted value for normal. Most papers cite gestation specific thresholds, with measurements between 4 and 10 mm in the second trimester and 7–10 mm in the third trimester [8–10]. The variation in diagnostic criteria is due to the difficulty in correlating antenatal sonographic findings with postnatal pathology and renal function, especially in cases of mild dilatation.

The likelihood of a significant postnatal renal anomaly increases proportionally with the severity of dilatation. Over 50% of cases with an APRPD $>$ 10 mm at 20 weeks will have a significant uropathy, increasing to 94% when the APRPD is $>$ 20 mm [8, 11, 12]. However, when using the strictest APRPD criteria above, a large proportion of antenatally diagnosed UTD will represent either transient or physiological dilatation that resolves after delivery [8, 10, 11]. Similarly, non-obstructing pathologies such as vesico-ureteric reflux (VUR) may also present with dilatation [13]. In cases of mild dilatation, only a minority of cases will represent a clinically significant obstructive uropathy. The incidence, pathophysiology and sonographic features of the different aetiologies of antenatal UTD are described in Table 1.

The goal of antenatal screening is to establish a suitable APRPD cut-off that demonstrates acceptable sensitivity in diagnosing uropathy, whilst avoiding unnecessary

Table 1 Aetiology of antenatal urinary tract dilatation

Condition	Epidemiology	Laterality	Pathophysiology	Sonographic features	Outcome
Transient/physiological	50–70%	Unilateral or bilateral	Possibly caused by a transient narrowing of the PUJ that resolves as the fetus matures	Often mild hydronephrosis	Spontaneous resolution
VUR	10–40% Male:female 1:2	60% bilateral	Hydronephrosis secondary to retrograde passage of urine from the bladder into the upper urinary tract	Hydronephrosis with a variable degree of dilatation. Antenatal diagnosis difficult May appear as VUJ obstruction or PUV if severe	Spontaneous resolution is likely, especially in mild cases [15].
PUJ dysfunction	10–30% Male:female 3:1	10–20% bilateral	Intrinsic stenosis (75%) or extrinsic compression (ureteric insertion anomalies or accessory renal arteries crossing).	Dilatation of the renal pelvis and calyces without dilatation of the ureters or bladder Severe obstruction can result in calyceal rupture and perinephric urinoma	20% will require surgical intervention [16]
VUJ dysfunction (non-refluxing megaureter)	5–15% Male:female 2:1	30–40% bilateral Left > right	Dysfunction in a localised region or physical obstruction in the distal ureter (stricture, atresia, vascular obstruction).	Hydronephrosis and ureteric dilatation (megaureter). Normal bladder and AFI	60% resolve spontaneously depending on cause and severity [17].
Multicystic kidney disease	2–5% Male > female	Usually unilateral	Form of renal dysplasia resulting in multiple non-communicating cysts.	Multiple non-communicating thin-walled cysts with no normal renal tissue. 'Cluster of grapes' appearance. The ureter is often absent. Associated renal and non-renal anomalies	Majority of affected kidneys will atrophy Poor prognosis in bilateral disease
Ureterocele (including ectopic ureter and duplex kidney)	2% Male:female 1:3	10–15% bilateral	Ureterocoeles are cystic dilatations of the terminal ureter within the bladder or urethra. Associated with duplex kidney (80-90%) and ectopic ureters (75%).	Hydronephrosis and hydroureter with presence of cystic structure in base of bladder More common in upper pole of duplex system	Majority require surgical management [18]
PUV	1% males only	Bilateral obstruction	Persistent urogenital membrane. Obstruction can be complete or partial.	Dilated thick walled bladder with dilated posterior urethra (key hole sign) Bilateral hydronephrosis and hydroureter. Liquor volume variable according to severity	Renal failure and pulmonary hypoplasia in severe cases [19]
Other urethral pathology (urethral atresia, megacystis micro-colon, congenital megalourethra)	Rare	Bilateral obstruction	Pathophysiology varies depending on condition.	Sonographic features of a lower urinary tract obstruction. Associated features depending on condition.	Many lethal or have a very poor prognosis

PUJ pelvi-ureteric junction, *VUR* vesico-ureteric reflux, *VUJ* vesico-ureteric junction, *PUV* posterior urethral valve

surveillance, investigation and treatment of those without significant disease.

In the UK the NHS Fetal Anomaly Screening Programme have recommended an APRPD of > 7 mm at the anomaly ultrasound performed between 18^{+0} and 20^{+6} weeks as a threshold for referral and further investigation [14]. In comparison, a consensus group in the USA have proposed a two-group classification. The low-risk group includes APRPD of 4 to < 7 mm in the second trimester, or 7 to < 10 mm in the third trimester. An APRPD of ≥ 7 mm in the second trimester or ≥ 10 mm in the third trimester represents a high-risk group [7]. The assigned

group dictates the frequency and degree of follow-up. Both systems require ongoing validation and clinical correlation with postnatal findings.

Antenatal Investigation and Management of Urinary Tract Dilatation

Due to the potential of an underlying uropathy, evaluation by a fetal medicine specialist is advised when UTD is diagnosed on antenatal ultrasound. The role of the specialist is to assess severity, consider any associated pathology and provide counselling regarding the likely prognosis, progression and treatment options.

Factors more predictive of severe disease include the degree of hydronephrosis, bilateral disease, oligohydramnios, additional renal anomalies (calyceal dilatation, parenchymal changes) and the presence of extra-renal anomalies [20–22].

Antenatal Ultrasound Surveillance

When isolated mild unilateral hydronephrosis (APRPD < 10 mm) is present at the mid-trimester scan, most authors agree that a single follow-up ultrasound in the third trimester is appropriate [7]. Transient hydronephrosis is common in this group, often resolving by the third trimester ultrasound, requiring no further antenatal or postnatal investigation [8, 23].

In cases where features of more severe disease are present, an individual approach to ultrasound surveillance should be adopted. Assessment every 2–4 weeks will detect progression of renal pelvis dilatation or changes in the amniotic fluid volume, that may prompt intervention. Iatrogenic preterm delivery for worsening renal disease is rarely indicated.

Associated Anomalies and Karyotyping

The association of isolated renal pelviceal dilatation with chromosome abnormalities is small. However, a thorough assessment for extra-renal anomalies is important to preclude UTD as a feature of a wider syndrome or association (e.g. VACTERL). Where extra-renal anomalies are detected in addition to UTD, invasive testing for fetal karyotyping and microarray should be offered.

Where isolated mild hydronephrosis is present, the decision to offer invasive testing should be made in the context of other clinical information, and should not be routinely offered if results from first trimester screening or non-invasive prenatal testing (NIPT) demonstrate a low risk for aneuploidy [24, 25].

Fetal Urinalysis

Biochemical markers excreted in the fetal urine can be sampled to provide an objective measure of renal function. Increased urinary sodium and beta-2-microglobulin have been used, although to date no single analyte has been able to reliably predict postnatal renal function and its use in clinical practice is often limited to situations where in utero fetal procedures are being considered [26].

In-Utero Fetal Procedures

In-utero fetal surgery has been used in the context of lower urinary tract obstruction (LUTO) usually secondary to either posterior urethral valves or urethral atresia. Vesicoamniotic shunting attempts to drain urine from the fetal bladder into the amniotic cavity, avoiding renal damage and oligohydramnios with its associated adverse effects on pulmonary development.

A randomised control trial (PLUTO) found that although shunting was associated with a trend towards increased neonatal survival (RR 1.88, 95% CI 0.71–4.96; $p = 0.27$), the survivors experienced significant short and long-term morbidity irrespective of treatment [27]. The shunting procedure was also associated with a significant risk of complication, including 3 out of 15 (20%) pregnancies lost as a result of the intervention [27].

Some studies have demonstrated the feasibility of fetoscopic cystoscopy in the treatment of LUTO [28, 29]. The procedure involves the insertion of a fibre-endoscope into the dilated urinary bladder, followed by identification and treatment of the obstruction with laser fulguration or stenting. Whilst observational studies have demonstrated possible benefit in comparison to vesicoamnitoic shunting [30], the procedure has not been the subject of randomised controlled studies and has largely been disregarded.

Termination of Pregnancy

Severe obstructive uropathy is associated with high rates of fetal mortality and morbidity. Adequate fetal urine production, particularly during the second trimester, is important for normal lung and limb development. Uropathy with oligohydramnios is associated with lung hypoplasia and carries a particularly poor prognosis [31].

In cases of untreated LUTO mortality is reported to be 50%, increasing to 80% where oligohydramnios is present. Long term morbidity is also high, with 25–30% of survivors progressing to end stage renal failure requiring dialysis and transplant [27, 31].

Counselling for families with a fetus affected by severe, early onset obstructive uropathy should reflect the likely underlying diagnosis and include a realistic discussion

regarding prognosis and the option of termination of pregnancy. Parents should be supported by a multi-disciplinary team of obstetricians, neonatologists and paediatric urologists to support their decision making. They should also be guided to high-quality patient information such as that found on *infoKID* (http://www.infokid.org.uk).

Should termination of pregnancy be undertaken, post-mortem examination and fetal karyotyping (if not already performed antenatally) should be discussed and offered.

Post-natal Investigations

A number of post-natal investigative algorithms are available; these vary in the threshold APRPD at which investigations are instigated and also in the timing and nature of the individual tests. In the UK, all newborns with an APRPD > 7 mm will undergo an initial physical examination, which may identify a urological abnormality such as a palpable kidney or bladder, and a postnatal ultrasound. Although the benefit is not absolutely clear, currently all newborns are placed on trimethoprim antibiotic prophylaxis (2 mg/kg/day) [32]. A summary of diagnostic tests available and their uses are outlined in Table 2.

In general, postnatal ultrasound is avoided in the first 48 h of life as falsely reassuring scans may result in this period of under-hydration and relative oliguria. However, a small number of newborns will require discussion with the paediatric urology service and more urgent ultrasound prior to discharge if there is a significant concern about potential obstructive uropathy. In our centre, indications for early ultrasound are as follows:

- Male infant with bilateral APRPD > 7 mm and hydroureter and/or abnormal bladder—risk of posterior urethral valve (PUV).
- Any infant with bilateral APRPD > 7 mm and hydroureter and large ureterocele—risk of prolapse.
- Any infant with bilateral APRPD > 20 mm—risk of bilateral pelvi-ureteric junction (PUJ) dysfunction.
- Any infant with unilateral APRPD > 30 mm—risk of unilateral PUJ dysfunction requiring early surgery.

Most usually ultrasound is performed at 1 and 6 weeks of age prior to outpatient review in the neonatal clinic. If both scans are normal, antibiotics are discontinued and the child is discharged; however, if either scan reveals persistent dilatation, then the child will subsequently be seen in the paediatric nephrology clinic and further investigations arranged. The precise indications for each investigation can vary, but in general, a micturating cystourethrogram (MCUG) will be recommended if ureteric dilatation is seen on ultrasound; dimercaptosuccinic acid (DMSA) radionuclide scan if the kidney is duplex or if VUR is identified on MCUG; and mercapto acetyl triglycerine (MAG3) scan if PUJ or vesico-ureteric junction (VUJ) dysfunction are likely. These second line investigations allow a specific urological diagnosis to be made, and subsequent management and follow-up can be tailored accordingly.

Specific Conditions

Pelvi-Ureteric Junction (PUJ) Dysfunction

Historically, dilatation secondary to narrowing or stenosis at the PUJ was referred to as PUJ 'obstruction'. However spontaneous resolution can occur in up to 25% of infants as the degree of stenosis improves [33, 34], and as a result the term PUJ 'dysfunction' is now preferred. In a series of patients from Great Ormond Street Hospital (GOSH), Dhillon et al. delineated the natural history of PUJ dysfunction (see Table 3), demonstrating that an increasing APRPD was associated with increased need for surgery, with pyeloplasty inevitable when the APRPD > 40 mm [34]. In the so-called 'grey zone' with an APRPD 20–30 mm, approximately 35% resolve; 25% remain static during follow up; and 40% require surgery. This work has formed the basis of number of follow up protocols,

Table 2 Diagnostic tests available in the postnatal assessment of obstructive uropathy

Investigation	Use
Ultrasound	Unilateral/bilateral dilatation; simplex/duplex system; APRPD; calyceal dilatation; ureteric dilatation (proximal and distal); bladder abnormalities
MCUG	Urethral anatomy; bladder abnormality; VUR
DMSA	Differential renal function and morphology: generally used in VUR
MAG3	Differential renal function and drainage: generally used in obstructive uropathy
MRU	Specialist investigation where anatomy is complex

APRPD anteroposterior renal pelvis diameter, *MCUG* micturating cystourethrogram, *VUR* vesico-ureteric reflux, *DMSA* dimercaptosuccinic acid, *MAG3* mercapto acetyl tri-glycerine, *MRU* magnetic resonance urography

Table 3 Likelihood of pyeloplasty in PUJ dysfunction by APRPD

APRPD (mm)	Risk of requiring pyeloplasty (%)
< 15	< 2
15–20	11
20–30	40
30–40	90
> 40	100

PUJ pelvi-ureteric junction, *APRPD* anteroposterior renal pelvis diameter

stratifying patients into risk groups using regular ultrasound and isotope studies.

Our local protocol includes an initial ultrasound and MAG3, then ultrasound every 3 months for the first year, every 6 months for the second year, and then annually until the age of 4 years. If the dilatation remains static during the first year of follow up, then a second MAG3 is recommended at 1 year to ensure maintained function, and the appropriateness of continued observation. We now consider pyeloplasty if the APRPD was > 30 mm; if the APRPD > 20 mm with marked calyceal dilatation on ultrasound; if the differential function on initial isotope study was < 40%; or if there was a drop in function on second isotope > 10% (e.g. from 48 to 43%).

Vesico-Ureteric Junction (VUJ) Dysfunction

The term VUJ dysfunction is applied to any dilated ureter > 7 mm in diameter, when there is no VUR identified on MCUG and poor drainage is seen on MAG3. Retrospective series demonstrate that the ureteric dilatation will improve spontaneously in one-third of cases, and remain static in a further one-third [35], and thus initial management is generally conservative [36], following similar protocols to those used in PUJ dysfunction.

The British Association of Paediatric Urologists recommend intervention if the distal ureter is > 10 mm and the child has symptoms such as febrile UTI or pain; if the differential function is < 40% or drops by > 10% on serial isotope studies; or if the dilatation progresses to > 15 mm even in the absence of symptoms [37]. Cystoscopy, ureteric dilatation and stenting is often possible and may prove to be a definitive intervention, with ureteric reimplantation an option if stenting fails.

Ureterocele

A ureterocele is a cystic dilatation of the intravesical ureter, usually associated with the upper pole of a duplex system (80–90%), and bilateral in 10–20% [12]. Although they usually remain entirely within the bladder, a large ureterocele may extend through the bladder neck and prolapse down the urethra, resulting in bladder outflow obstruction, and thus prompt ultrasound assessment is recommended in any infant with bilateral dilatation and a large ureterocele. An MCUG is generally performed to look for VUR into the lower pole of an associated duplex, and a DMSA to assess function, although there is often very little in the upper pole of a duplex. Definitive surgical treatment usually comprises an upper-pole heminephrectomy, but transurethral cystoscopic puncture of the ureterocele would be performed urgently if bladder outflow obstruction has occurred.

Posterior Urethral Valves (PUV)

PUV is the most common cause of severe obstructive uropathy. In all suspected cases, a urethral catheter should be passed promptly after delivery and subsequent fluid management is critical as a post-obstructive diuresis may ensue. Neonates with severe bilateral renal dysplasia may also need support for associated pulmonary hypoplasia. If it is not possible to catheterise the bladder urethrally, then a suprapubic catheter should be inserted.

Ultrasound should be performed urgently within 48 h, and an MCUG once the child is stable. Cystoscopic valve ablation (using cold knife or cautery) is usually undertaken within the first week. Vesicostomy formation may be required in pre-term infants < 2.5 kg if they are too small for a cystoscopic procedure. Circumcision is usually recommended as it reduces the incidence of UTI by > 80% [38]. Long term follow-up involving both paediatric nephrology and urology is essential, as 20–30% will develop end stage renal failure requiring renal replacement therapy or transplant [39].

Summary and Conclusion

A structured and evidenced based approach to the ultrasound assessment of dilatation of the fetal urinary tract is required. International variation remains in the clinical criteria and APRPD cut-offs used in the diagnosis of the condition. Consensus and validation of the current diagnostic algorithms are required to ensure a balance between reliable detection of obstructive uropathy, whilst avoiding unnecessary surveillance and treatment in cases of transient or physiological dilatation.

The importance of antenatal diagnosis cannot be understated, as it allows for realistic prognostication and prompt neonatal intervention when required.

The post-natal management of obstructive uropathy is dependent on the underlying aetiology. Available

investigations should be used to identify those children that would benefit from surgical intervention.

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