Fetal bladder outlet obstruction: evaluation and treatment
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Background: Fetal renal anomalies
• 15-20% of all congenital defects
• Prenatal detection of renal abnormalities occurs in 0.1-0.4%
• More common in males than females (2.5:1)
• Abnormalities range from mild to severe

Etiology
• Majority of renal anomalies ae isolated
  • Low risk of aneuploidy or genetic syndromes
• Polycystic kidneys
  • Autosomal recessive or autosomal dominant
• Other genetic syndromes
  • Multicystic or polycystic kidneys

Overview of Fetal GU anomalies

Ultrasound evaluation kidneys

Ultrasound evaluation of bladder in first trimester
1st trimester identify fetal bladder and kidneys (more echogenic and easy to see
Color flow of umbilical arteries also useful)
Embryology of fetal GU tract

- 3 sets of successive kidneys
  - Pronephros - rudimentary
  - Mesonephros - 5th – 12th week
    - Mesonephric duct gives rise to ureteral bud + ureter, collecting tubules and renal pelvis
  - Metanephros primordia of permanent kidneys

Development of permanent kidneys

- 2 sources
  - Ureteric bud
  - Metanephrogenic blastema
- Ureteric bud elongates and penetrates blastema
  - Stalk forms ureter
  - Cranial part branches forming collecting tubules and calyces

Positional changes of kidneys

Development of Urinary Bladder

- Urogenital sinus is divided into 3 parts
- Vesical part forms most of bladder and is continuous with allantois
- Pelvic part becomes
  - Urethra in the neck of the bladder
  - Prostatic part of the urethra in males
  - Entire urethra in females
- Phallic part that grows toward genital tubercles (primordium of penis or clitoris)

Development of Urethra

- Females: urogenital sinus
- Males: urogenital sinus + ingrowth of ectodermal cells

Amniotic fluid

- Early amniotic fluid
  - Placental surface
  - Transmembranous passage across amnion
  - Surface of embryo

Fetal urine production

Structural or functional defects of urinary tract lead to decreased AF and identification of anomalies
Fetal hydronephrosis

- Most common birth defect (0.5-5%) pregnancies
- High sensitivity, low specificity
- >50% transient or physiologic

Differential diagnosis

**Obstructive**
- Ureteropelvic junction obstruction
- Ureterovesical junction obstruction
- Multicystic dysplastic kidney
- Ureterocele
- Duplicated collecting system
- Posterior urethral valves
- Ectopic ureter
- Urethral atresia
- Sacrococcygeal teratoma
- Hydrometrocolpos

**Non-Obstructive**
- Vesicoureteral reflux
- Physiologic dilation
- Prune-Belly syndrome
- Renal cystic diseases

Classifications

- Renal Pelvic Diameter (RPD)
- Society of Fetal Urology (SFU) criteria
- Urinary Tract dilation (UTD) classification system

Renal Pelvic Diameter

- Measures collecting system only
- No consensus on threshold RPD that defines clinically significant fetal hydronephrosis and need for post-natal follow-up
  - 4-5mm lowest cut-off
  - 4 – 10mm mild
  - > 10mm in 2nd and >15mm in 3rd

Society of Fetal Urology (SFU)

- Antenatal (A) and Postnatal (P) classification
- Based on US findings, stratified by GA and whether A or P
  - Anterior and posterior RPD (APRPD)
  - Calyceal dilation
  - Renal parenchymal thickness
  - Renal parenchymal appearance
  - Bladder abnormalities

Urinary tract dilation (UTD) classification system

- Normal: APRPD
  - < 4mm 16 – 27 w
  - < 7mm at ≥ 28 w
- A1:
  - 4 – 7mm APRPD at 16-27 w
  - or 7 to <10 mm at ≥ 28 w
  - with or w/o central calyceal dilation
- A2-3:
  - APRPD ≥ 7mm at 16-27 w
  - or ≥10mm at ≥28 weeks, peripheral calyceal dilation, ureteral dilation, renal parenchymal or bladder abnormalities

Add descriptions: SFU grade 4 L/R hydronephrosis, SFU grade 4 L/R hydronephrosis
What class?

16-27 weeks
APRPD 4-7mm
Central calyceal dilation

≥ 28 weeks
APRPD ≥10 mm
Central calyceal dilation

Natural history

• Mild – 88% resolve in fetal/neonatal period
• Moderate- severe: 30% persisting in 3rd trimester require postnatal surgery

Evaluation of fetal hydronephrosis

• Severity and bilaterality increase risk of congenital anomalies of kidney and urinary tract
• Repeat US in 3rd trimester – prognosis for intervention postnatally

Hydroureter

• Vesicoureteral reflux (VUR)
• Obstruction distal to ureteropelvic junction (ureterocele, megaureter, posterior urethral valves)
Ureterocele

- Cystic dilation of distal intravesical portion of the ureter
- Often at orifice draining upper pole of duplicated kidney

Renal parenchyma

- Thinning
  - < 3mm
  - Does not necessarily correlate with poor renal function
- Cortical cysts
- Echogenic kidneys

LUTO: lower urinary tract obstruction

- Bladder thickness – obstruction distal to bladder
- Keyhole sign
- Bladder enlargement: sagittal diameter of GA weeks (mm) + 2 mm
- Often PUV
- Urethral atresia
- Look for ureteroceles

Diagnosis of LUTO

- 1/5,000 – 1/25,000 pregnancies
- Markedly distended bladder often with thickened wall
- Dilated ureter and calyces – 40-50% LUTO
- Cortical cysts, hyperechoic kidneys – end stage
- Differential diagnosis
  - PUV – males
  - Urethral atresia – females
    - Zygomatic osteoma
    - Caudal regression
  - Mega-cystis–microcolon-intestinal hyperperistalsis syndrome
  - Ureterocele
Differential diagnosis

• Prune-Belly syndrome
• Lax or absent abdominal wall muscles
• Thin-walled bladder
• Cryptorchidism
• Aneuploidy (most common trisomies 13, 18, 21)
• Megacystis-megaureter syndrome (severe vesicoureteral reflux)
• Megacystis-microcolon syndrome (thin walled bladder w/o dilated posterior urethra, normal or increased AF)
• In female fetus dilated vagina due to septal anomaly can mimic dilated bladder
• Persistent cloaca

27% of prenatal diagnoses of LUTO were false positives – most common postnatal diagnoses (Vesicoureteral reflux (25%), cloacal dystrophy (19%), hydronephrosis (3%) and some resolved.

Evaluation of LUTO

• Anatomic survey
• Fetal echocardiogram
• AF volume assessment
• Genetic testing (10% associated with Trisomies 13, 18, 21)
• U/I assessments
• With oligohydramnios and desire for possible intervention, assess renal function

Evaluation of fetal urine

• 2 - 3 consecutive vesicocenteses
  • 22g spinal needle
  • Color flow to avoid umbilical arteries
  • 1st bladder tap
    • Can send for genetic evaluation (CMA)
    • +/- electrolyte analysis
  • 2nd bladder tap
    • 24-48 hours later
    • Na, Cl, Osm, Ca, Beta-2 microglobulin

Fetal urine isotonic and progressively becomes more hypotonic – use GA cut-offs. May not necessarily reflective of renal function at birth despite intervention.

32% of prenatal diagnoses of LUTO were false positives – most common postnatal diagnoses (Vesicoureteral reflux (25%), cloacal dystrophy (19%), hydronephrosis (3%) and some resolved.

Management of LUTO

• Multidisciplinary counseling
• Pregnancy termination should be offered
• Serial assessment of fetal renal function

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• Calcium and sodium > 95%ile for GA – best predictors for abnormal post-natal renal function
• Due to small study samples and varying thresholds of urinary markers, fetal urine analysis is not that helpful in predicting postnatal renal outcome.

Proteomic approach: 12 peptides in fetal urine were predictive of developing end-stage renal disease

Fetal serum beta-2 microglobulin better correlated with postnatal serum creatinine

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Treatment

• Indications
  • Male fetus
  • Second trimester
  • Bilateral disease
  • Reasonable fetal urinary studies
  • Progressive oligohydramnios

• Options
  • Vesico-amniotic shunting
  • Valve ablation via cystoscopy
  • Vesicostomy
  • Serial amnioinfusion
Vesico-amniotic shunting

• Technique
  - Seldinger technique
  - Pigtail shunt (Rodeck, Rocket, Harrison)
• Complications
  - Shunt blockage, migration
  - Preterm labor, urinary ascites, infection, IUD

Vesicoamniotic shunt did not increase survival to 28 days in intent-to-treat analysis but did increase survival based on actual treatment.

• High morbidity and mortality in both groups
• High rate of shunt complications

Trial stopped early due to poor recruitment

Analysis based on RR: benefit of shunt on survival at:

- 28 days (RR 3.2, 95% CI 1.06-9.62)
- 1 year (RR 4.27, 95% CI 1.07-16.96)
- 2 years of age (RR 6.27, 95% CI 1.07-16.96)

3/12 who survived to age 2 had no renal impairment

Long-term outlook is poor

Technical failure with fetal cystoscopy (FC)

No valid proof of superiority of FC vs vesicoamniotic shunt (VAS)

VAS may not improve kidney function and may worsen urologic function

FC limited by technical factors and lack of reproducibility

High perinatal morbidity and mortality

Poor prognostic features
  - Renal parenchymal abnormalities
  - Abnormal fetal urinanalysis
  - Early, severe oligohydramnios with pulmonary hypoplasia
  - High change of ESRD requiring dialysis and transplant
  - May have bladder damage and need for self-catheterization or bladder surgeries

Renal pelvicoal dilation/hydronephrosis

Mild – 88% resolve in fetal/neonatal period
  - Moderate-severe: 30% persisting in 3rd trimester require postnatal surgery

UTD classification helpful in communication between subspecialties

LUTO

Currently no evidence of superiority of cystoscopy over VAS