بسم الله الرحمن الرحيم

PEDIATRICS **Nephrology**

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Urinary Tract Infections (UTI)

Prevalence

- The prevalence of UTI is 1-3% in girls & 1% in boys.
- In girls, the first UTI occurs by the age of 5 years, with peaks during infancy & toilet training.
- In boys, it is mostly during the 1st year of life. It is much more common in uncircumcised boys.
- The prevalence of UTI varies with age. During the 1st year of life, male:female ratio = 2.8 - 5.4:1. Beyond 1-2 years of life, male:female ratio= 1 : 10.

Etiology

- UTI is mainly caused by colonic bacteria.
- The most common bacteria in females is E.Coli (75-90%) followed by klebsiella & proteus.
- In males, some reports say that after 1st year of life, proteus= E.coli. Other reports reveals the preponderance of G+ve bacteria.
- Staphylococcus saprophyticus & enterococcus are a pathogen of both sexes.
- There may be viral causes of UTI ,especially adenoviruses which usually cause cystitis.
- UTI have been considered as an important risk factor for the development of renal insufficiency or end-stage renal disease, but only 2% of current renal insufficiency report a history of UTI which may be due to better recognition of the risk of UTI & prompt diagnosis & treatment. Furthermore, many children receive antibiotics for fever without a focus resulting in partially treated UTI.

Clinical manifestations & classification

There are 3 basic forms of UTI :

1. ***Pyelonephritis :*** It is characterized by any or all of the following symptoms : abdominal or flank pain, fever, rigor, malaise, nausea, vomiting, & occasionally diarrhea. Fever may be the only manifestation. Newborns can show nonspecific symptoms as jaundice, poor feeding, irritability & weight loss. Pyelonephritis is the most common serious bacterial infection in infant <24 mo of age who have fever without an obvious focus. Acute pyelonephritis can result in renal injury which is called " pyelonephritic scarring". Acute lobar nephronia (acute lobar nephritis) is a renal mass caused by acute focal infection without liquefaction. It may be an early stage of renal abscess. Perinephric abscess can develop also.

2. ***Cystitis :*** Symptoms include dysurea, urgency, frequency, suprapubic pain, incontinence, & malodorous urine (not specific for UTI). It is usually without fever or renal injury. Acute hemorrhagic cystitis is often caused by E.coli & may be attributed to adenovirus.
3. ***Asymptomatic bacterurea :*** It is defined as a +ve urine culture without symptoms & occurs almost exclusively in females. This condition is benign & does not cause renal injury except in pregnant women in whom if untreated, it can → symptomatic UTI.

Pathpgenesis & pathology

Nearly all UTI^S are ascending infections. The bacteria arise from the fecal flora, colonize the perineum, & enter the bladder via the urethra. In uncircumcised males, the bacteria arise from the flora beneath the prepuce . In some cases , the bacteria ascend to the kidney to cause pyelonephritis. In rare cases, renal infections may occur by hematogenous spread.

● ***Risk factors for UTI : These include :***

•Female sex • Uncircumcised male • Vesicouretric reflux • Toilet training : In female, UTI often occur at the onset of toilet training due to voiding dysfunction which occurs at that age (incomplete bladder emptying). • Obstructive uropathy → hydronephrosis (urinary stasis). • Urethral instrumentation : during voiding cystourethrogram or non-sterile catheterization. • Wipping from back to front. • Tight clothing (underwear). • Pinworm infestation. • Constipation which may → voiding dysfunction. • P fimbriated bacteria :There are 2 types of pilli or fimbriae on the bacterial surface 1 & 2. Type 2 fimbriae which is found on some strains of E.Coli & can be agglutinated by P blood group RBC^S, are more likely to cause pyelonephritis. • Anatomic abnormalities as labial adhesion. • Neuropathic bladder : incomplete bladder emptying & detrusor-sphincter dyssenergia. • Sexual activity : in female due to incomplete bladder emptying. • Pregnancy : 4-7% have symptomatic bacterurea which may → UTI. • Breast feeding → ↓ UTI.

Diagnosis

- UTI may be suspected based on symptoms or findings on urinalysis, or both; *a urine culture is necessary for confirmation and appropriate therapy*.
- There are several ways to obtain a urine sample; some are more accurate than others.
- In toilet-trained children, a midstream urine sample usually is satisfactory; the introitus should be cleaned before obtaining the specimen. In uncircumcised boys, the prepuce must be retracted; if the prepuce is not retractable, a voided sample may be unreliable and contaminated with skin flora.
- In children who are not toilet trained, a catheterized urine sample should be obtained. Alternatively, the application of an adhesive, sealed, sterile collection bag after disinfection of the skin of the genitals can be useful only if the culture is negative or if a single uropathogen is identified. However, a positive culture can result from skin contamination, particularly in girls and uncircumcised boys.
- If treatment is planned immediately after obtaining the urine culture, a bagged specimen should not be the method because of a high rate of contamination often with mixed organisms.
- A suprapubic aspirate generally is unnecessary.

- Prompt examination of the urine sample is important, because if urine remains at room temperature > 60 minutes → overgrowth of a minor contaminant, so, the sample should be stored in the refrigerator.
- The sample for GUE should be obtained from the same specimen as that cultured.
- Pyurea (WBC^S in urine) suggests infections, but infections can occur without pyurea & vice-versa.
- **Sterile pyuria** (positive leukocytes, negative culture) occurs in partially treated bacterial UTIs, viral infections, renal tuberculosis, renal abscess, UTI in the presence of urinary obstruction, urethritis due to a sexually transmitted infection (STI), inflammation near the ureter or bladder (appendicitis, Crohn disease), and interstitial nephritis (eosinophils).
- Nitrates & leukocytes esterase tests are usually +ve in infected urine.
- Microscopic hematurea is common in acute cystitis.
- WBC casts in the urinary sediments suggest renal involvement (but these are rare).
- With acute renal infection → leucocytosis, neutrophilia, ↑ESR & CRP.
- With renal abscess → WBC > 20,000 - 25,000/mm^3.
- Blood culture is indicated with suspicion of sepsis which is common in pyelonephritis especially in infants & in any child with obstructive uropathy.
- If the child is asymptomatic & GUE is normal → UTI is unlikely.
- If the child is symptomatic & GUE is normal → UTI is likely.
- If the culture shows >100,000 colonies of a single pathogen, or if there are 10,000 colonies and the child is symptomatic, the child is considered to have a UTI. In a bag sample, if the urinalysis result is positive, the patient is symptomatic, and there is a single organism cultured with a colony count >100,000, there is a presumed UTI. If any of these criteria are not met, confirmation of infection with a catheterized sample is recommended.

Treatment

■ *Cystitis :* The choice of the suitable antibacterial drug should ideally based on the result of urine C & S, however, in acute severe conditions, treatment should begin without waiting for results (empirical therapy). The course is that of 3-5 days or ,some times, 7-10 days of (one) the following oral antibiotics :

- Trimethoprim-sulfamethaxasole, 4-6 mg trimethoprim / kg / day, divided into 2 doses,
- Nitrofurantoin, 5-7 mg / kg / day, in 3-4 divided doses. It should not be used with the febrile UTI because it does not achieve significant renal tissue level.
- Amoxicillin, 50 mg / kg /day, in 2-3 divided doses.

■ *Acute pyelonephritis :* The course is that of 14 days of one of the following parenteral antibiotics :

- Ceftriaxon, 50-75 mg / kg / day (not more than 2 gm / day).
- Ampicillin, 100 mg / kg / day + Gentamicin, 3-5 mg / kg /day, in 1-3 divided doses. (S/E of gentamicin include : ototoxicity & nephrotoxicity. Serum creatinine & gentamicin level must be obtained before treatment then daily assessment. Aminoglycosides are particularly effective against pseudomonas & alkallinization of urine with NaHCO3 → ↑ their effectiveness in the urinary tract).
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Other oral antibiotics include one of the following :

- Oral 3rd generation Cephalosporin as Cefixime, 8 mg / kg / day, in 1-2 divided doses. This drug may be the drug of choice of oral treatment. It is not effective against pseudomonas.
- Oral Ciprofloxacin, 15-30 mg / kg / day, in 2 divided doses , is an alternative drug for resistant organisms especially pseudomonas in patients > 17 years & in patients < 17 years with cystic fibrosis, pulmonary infections secondary to pseudomonas, & occasionally for children with pseudomonas UTI (S/E of ciprofloxacin → potential cartilage damage in children → restricted use).
- Some times, with febrile UTI, a loading dose of IM Ceftriaxon followed by oral 3rd generation Cephalosporins is effective.

■ *Renal or peri-renal abscess or infections with obstructive uropathy* → surgical or percutanous drainage + antibiotics + other supportive treatment.

Notes → 1. Urine C&S should be performed 1 week after the termination of treatment of any UTI 2. Follow-up urine culture should be performed periodically for 1-2 years even with asymptomatic child.

■ *Supportive therapy :*

- ↑ fluid intake.
- Antipyretics as Paracetamol, 10 mg/kg/dose, 4-6 times per day or Iboprufen 10-15 mg/kg/dose, 3-4 times per day.
- Bladder analgesics may be used in older children to relief pain associated with severe dysurea as Phenazopyridine (Urisept, tab.=100 mg), 10mg/kg/day, in 3 divided doses.
- Alkalinizing agents as NaHCO3 or Na-citrate are especially useful with aminoglycosides. The dose is one teaspoon of granules+some water, 2 times per day.

■ *Long term antibiotics prophylaxis :*

It is the prophylaxis against re-infection using either Trimethoprim-Sulfamethoxasole or Nitrofurantoin at 1/3 of the therapeutic dose once a day which is often effective. Prophylaxis with Amoxicillin or Cephalexin may be inappropriate because of the rapid development of bacterial resistance. A 6-12 months course is indicated. If infection recurs after stopping prophylaxis, antibiotics should be resumed. Indication for antibiotics prophylaxis are :

1. Infants or children with their 1st UTI, who have finished their course of treatment & waiting for completion of other studies as voiding cystourethrography(VCUG) or renal ultrasound
2. Patients with known urologic abnormalities which place them at high risk of recurrent UTI as neurogenic bladder, urinary tract stasis & obstruction, vesico-uretral reflux(VUR), calculi & posterior urethral valve(PUV).
3. Children & adolescents with recurrent UTI & normal urinary tract anatomy.

■ *Treatment of consequences* of chronic renal damage caused by pyelonephritis as hypertension & renal insufficiency.

Imaging studies

The goal of imaging studies in children with UTI is to identify the anatomic abnormalities which predispose to infection :

1. *Renal ultrasound :* It should be obtained to rule out : • Hydronephrosis • Renal or perirenal abscess • Acute pyelonephritis in 30-60% of cases by demonstrating enlarged which may require prompt drainage of the collecting system by percutanous nephrostomy.
   Normally, the difference in renal lengths of 2 kidneys is <1 cm & large disparity may → impaired renal growth. Renal ultrasound can be done with other studies or at time of hospital admission if the patient appears toxic, or hypertensive, or if there is evidence of ↓ renal function.

2. *Voiding cystourethrogram (VCUG) :* It is indicated in the following conditions :
   - All children < 5 years of age.
   - Any child with febrile UTI.
   - School aged girls with ≥ attacks of UTI.
   - Any male with UTI.

   ■ The most common finding is vesico-ureteric reflux (VUR) which is identified in about 40% of cases.
   ■ Timing of VCUG is controversial. In some centers , the study is delayed for 2-6 weeks to allow the inflammation in the bladder to resolve, however, the incidence of VUR is identical, irrespective of whether the VCUG obtained during treatment or after 6 weeks , so obtaining VCUG before discharging from the hospital is recommended.

3. *Technitium-labeled DMSA (dimercaptosuccinic acid) or glucoheptonate :* It is useful when the diagnosis of acute pyelonephritis is uncertain.
   - If VUR is present, the DMSA scan often is performed to asses whether renal scarring is present. The DMSA scan is the most sensitive & accurate study for demonstrating scarring.
4. *Excretory urography :* It is not as sensitive as the DMSA scan in demonstrating renal scarring, in addition, the visualization of the collecting system in infants & young children often is suboptimal, there is high risk of contrast allergy, & it can take 1-2 years for renal scar to appear in urogram.
5. *Computed tomography :* It may demonstrate acute pyelonephritis & renal scarring.

ENURESIS

Enuresis is urinary incontinence in a child who is considered adequately mature to have achieved continence. It is the most common urologic condition in children. Enuresis is classified as **nocturnal** (nighttime – majority of cases – good prognosis) or **diurnal** (daytime+ nighttime – more severe – less favorable prognosis). Daytime dryness is expected in the U.S. by age 4 years. Nighttime dryness is expected by age 6 years. Another useful classification of enuresis is **primary** (incontinence in a child who has never achieved dryness – 80% of cases) and **secondary** (incontinence in a child who has been dry for at least 6 months – 20% of cases). The prevalence of enuresis at age 5 yr is 7% in males and 3% in females. At age 10 yr, it is 3% in males and 2% in females, and at age 18 yr, it is 1% in males and extremely rare in females. Evidence suggests different rates of bed-wetting by ethnicity and culture.

Etiology: Enuresis is a symptom with multiple possible etiologic factors, including developmental difference, organic illness, or psychological distress.

A. Primary enuresis :

1. Maturational delay : Primary nocturnal enuresis due to maturational delay is by far the most common type of enuresis. It is 3 times commoner in boys than in girls & it is also commoner in the first born child & in low socioeconomic classes. A strong family history is present. The severity of enuresis is variable from one child to another but daily wetting is common in most cases & the condition may be exaggerated by parental punishment. On the other hand, understanding, encouragement & simple reward may be helpful.The prognosis for ultimate recovery is excellent.

2. Organic causes : They account for only small number of cases but they should be routinely excluded. Mental retardation, sacral anomalies(spina bifida, meningocele) & urological anomalies (bladder neck or urethral anomalies) are the main causes. In these cases, enuresis is commonly severe & diurnal.

B. Secondary enuresis : It is mostly nocturnal & caused by either emotional stress or organic causes :

1. Emotional stresses : Death of a parent, birth of a new sibling, move to a new house or marital conflicts are commonly responsible for secondary enuresis. Detailed environmental history is important in every case of secondary enuresis.

2. Organic causes : polyuria & urinary tract infection should be routinely excluded in every case of secondary nocturnal enuresis. History of dysuria or weight loss are particularly important. Urine examination should be a routine step.

Treatment : Treatment of underlying organic causes of enuresis, including UTIs, diabetes mellitus, sleep disorders, and urologic abnormalities, is essential. Elimination of underlying chronic constipation is often curative. Treatment options include **conditioning therapy**, **pharmacotherapy**, and **hypnotherapy** :

1. **Conditioning therapy :** The most widely used **conditioning therapy** for nocturnal enuresis is the **enuresis alarm**. Enuresis alarms have an initial success rate of 70% with a relapse rate of 10%. The use of an alarm requires commitment from the parent and the child. The alarm has a probe that is placed in the underpants or pajamas in front of the urethra. Children with daytime enuresis and small bladder capacity often are treated with **bladder stretching exercises**, in which the child is asked to practice holding urination for longer and longer periods. A reward system often is used in conjunction with this practice. Anticholinergic drugs, such as oxybutynin (5 mg two to three times a day for children 5 years and older) often are used for 2 to 3 months during "bladder stretching."

2. **Pharmacotherapy :** for nighttime enuresis includes tricyclic antidepressants and desmopressin acetate. **Imipramine** reduces the frequency of nighttime wetting. The initial dose for children 6 years and older is 25 mg 1 hour before bedtime. The dose may be increased to 50 mg after 1 week. The maximum dose for children younger than 12 years is 50 mg; it is 75 mg for those 12 years and older. The initial success rate is 50% with a relapse rate of 30% or more even after 6 months of treatment. The most important contraindication is risk for overdose (associated with fatal cardiac arrhythmia). **Desmopressin** is also used to treat enuresis and has proved to be safe. It is available in an oral form, which is more acceptable than the nasal spray formulation. The oral medication is started at 0.2 mg per dose (one dose at bedtime) and on subsequent nights is increased to 0.4 mg and then to 0.6 mg if needed. This treatment must be considered symptomatic, not curative, and has a relapse rate of 90% when the medication is discontinued.

3. **Hypnotherapy :** has a reported 44% success rate without relapse; an additional 31% showed significant improvement in the number of dry nights. Hypnotherapy for enuresis should be offered by health or mental health professionals who are qualified to evaluate and treat enuresis by other modalities and who have training in pediatric hypnotherapy.

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