

Urinary Tract Infection in Children: A Review

Farzana Hamid¹, Md. Rafiqul Islam², Nibedeta Paul³, Nadia Nusrat⁴, Rafia Parveen⁵

Abstract

Urinary tract infection (UTI) is one of the most common paediatric infections. By the time children are 5 years old, about 8% of girls and about 1-2% of boys have had at least one episode of UTI. UTIs are caused mainly by colonic bacteria, such as Escherichia coli, followed by Klebsiella and Proteus. However, any organism that gains access to the urinary tract system may cause infection, including fungi (Candida species) and viruses. In some instances, UTI results in recognition of an important underlying structural abnormality of the urinary tract. The febrile infant or child with clinically significant bacteriuria and no other site of infection to explain the fever, even in the absence of systemic symptoms has UTI. Signs and symptoms of UTIs vary depending on the child's age and on which part of the urinary tract is infected. The diagnosis of UTI is based on routine microscopic examination and culture of a properly collected urine specimen. Imaging studies are done in selected patients to identify anatomic abnormalities. Most cases of uncomplicated UTI respond readily to outpatient antibiotic treatment without further sequelae. All patients should have close follow-up to evaluate response to antibiotics and to prevent the development of long term complication.

Keywords: UTI; children; bacteriuria.

Delta Med Col J. Jul 2013;1(2):51-57

1. Associate Professor, Dept. of Pediatrics, Delta Medical College, Dhaka, Bangladesh.
2. Professor & Head of the Department, Dept. of Pediatrics, Delta Medical College, Dhaka, Bangladesh.
3. Assistant Professor, Dept. of Pediatrics, Delta Medical College, Dhaka, Bangladesh.
4. Registrar, Dept. of Pediatrics, Delta Medical College, Dhaka, Bangladesh.
5. Assistant Professor, Dept. of Radiology & Imaging, Delta Medical College, Dhaka, Bangladesh.

Correspondence: Dr. Farzana Hamid. e-mail: drfarzanahamid@yahoo.com

Introduction

Urinary tract infection (UTI) is a problem that is frequently encountered by paediatric healthcare providers. Over recent decades, the importance of UTI has been increasingly recognized, in particular the role of UTI as an occult cause of febrile illness in young children. Although UTIs do not occur with as great a frequency in children as in adults, they can be a source of significant morbidity in children. For reasons that are not yet completely understood, a minority of UTIs in children progress to renal scarring, hypertension and renal insufficiency.¹

Clinical presentation of UTI in children may be nonspecific and the appropriateness of certain diagnostic tests remains controversial. Studies have

shown that UTI may often be missed on history and physical examination, and the decision to screen for UTI must balance the risk for missed infections with the cost and inconvenience of testing. Interpretation of rapid diagnostic tests and culture is complicated by issues of contamination, false test results, and asymptomatic colonization of the urinary tract with nonpathogenic bacteria.²

The diagnostic work up should be tailored to uncover functional and structural abnormalities such as dysfunctional voiding, vesicoureteral reflux and obstructive uropathy. A more aggressive work-up, including ultrasound and voiding cystourethrography, renal cortical scintigraphy, is recommended for

patients at greater risk for pyelonephritis and renal scarring, including infants less than one year of age and all children who have systemic signs of infection concomitant with a UTI.³ Antibiotic prophylaxis is used in patients with reflux or recurrent UTI who are at greater risk for subsequent infections and complications.^{1,2}

The goal of this review is to provide an up to date summary of the literature with particular attention to practical questions about diagnosis and management for the clinician.

Epidemiology

The epidemiology of UTI during childhood varies by age, gender, and other factors. UTIs occur in as many as 5% of girls and 1 to 2% of boys. The incidence of UTI is highest in the first year of life for all children (1%) and the incidence in infants ranges from approximately 0.1-1.0% in all newborn infants to as high as 10% in low birth weight infants. Infection of the urinary tract before age one occurs more frequently in boys than in girls. After age one, both bacteriuria and UTI are more common in girls.⁴⁻⁶

Estimates of UTI incidence among infant boys have varied in different populations, likely due to factors such as circumcision, which has been associated with a reduction in risk of UTI. Another issue affecting estimates of incidence is the increased recognition of UTI as a potential source of febrile illness in young children. Screening studies in emergency departments suggest that up to 5% of children under the age of 2 presenting with fever have UTI, and over half of these would have been given alternative diagnoses such as otitis media had the urine not been screened as part of the study. Studies from Sweden have indicated that at least 3% of girls and 1% of boys have a symptomatic UTI by age 11 years. Other data, however, have suggested that 8% of girls have a symptomatic UTI during childhood and that the incidence of a first time UTI in boys older than 2 years is probably less than 0.5%. In sexually active teenaged females, the incidence of UTIs approaches 10%.^{6,7}

Definition of UTI

Urinary tract infection (UTI) is defined as the presence of bacteria in urine along with symptoms of infection. The three basic categories of UTI are pyelonephritis (upper UTI), cystitis (lower UTI) and asymptomatic

bacteriuria. The febrile infant or child with clinically significant bacteriuria and abdominal or flank pain, malaise, nausea, vomiting has pyelonephritis.^{1,4}

Children with UTIs, who have voiding symptoms or dysuria, little or no fever, and no systemic symptoms, have lower cystitis. After age 2 years, UTI manifesting as cystitis is common among girls. Children with a positive urine culture without any manifestation of infection have asymptomatic bacteriuria.²

Etiology & Pathogenesis

Almost all UTIs are ascending in origin. Most infections begin in the bladder; from there, pathogens can spread up the urinary tract to the kidneys (pyelonephritis) and possibly to the bloodstream (bacteremia). Most episodes of UTI during the first year of life are pyelonephritis.² Simple cystitis may progress to pyelonephritis. Predicting which patients will develop pyelonephritis is difficult, although evidence suggests that genetics may play a role. Bacterial infections are the most common cause of UTI, with *Escherichia coli* being the most frequent pathogen, causing 75-90% of UTIs.³

Other bacterial sources of UTI include *Klebsiella* species, *Proteus* species, *Enterococcus* species, *Staphylococcus saprophyticus* - especially among female adolescents and sexually active females, *Streptococcus group B* - especially among neonates, *Pseudomonas aeruginosa*, Fungi (*Candida* species) - especially after instrumentation of the urinary tract and Adenovirus rarely. After birth, the periurethral area, including the distal urethra, becomes colonized with aerobic and anaerobic microorganisms that appear to function as a defense barrier against colonization by uropathogens. In early childhood, enterobacteria and enterococci are part of the normal periurethral flora. *Escherichia coli* is the dominant gram-negative species in young girls, whereas *Escherichia coli* and *Proteus* species predominate in boys.⁵

Urine in the proximal urethra, urinary bladder, and other proximal sites in the urinary tract are normally sterile. Because normal voiding usually results in an essentially complete washout of contaminating bacteria and successful pathogenic colonization of the urinary bladder is unlikely unless bladder defense mechanisms are impaired. Therefore, disturbance of the normal periurethral flora predisposes a person to UTI. Entry of bacteria into the urinary bladder can

result from turbulent flow during normal voiding, voiding dysfunction, or catheterization. More rarely, the urinary tract may be colonized during systemic bacteremia (sepsis); this usually happens in infancy.⁷

Evidence suggests that genetics may play a role in the progression of simple cystitis to pyelonephritis. The identification of a genetic component may allow the identification of at-risk individuals and, therefore, prediction of genetic recurrences in their offspring. Thus far, 6 genes investigated in humans may be associated with susceptibility to recurrent UTIs; these are HSPA1B, CXCR1, CXCR2, TLR2, TLR4 and TGF β 1.⁸

The virulence of the invading bacteria and the susceptibility of the host are of primary importance in the development of UTI. Any condition that leads to urinary stasis (renal calculi, obstructive uropathy, vesicoureteral reflux and voiding disorders) may predispose to the development of UTI in children.^{4,9} Renal parenchymal infection and scarring are well established complications of infection of the upper urinary tract in children and can lead to renal insufficiency, hypertension and renal failure.¹⁰ Parenchymal scarring develops in 10-15% of children with UTI. Children less than one year of age with a UTI are at much greater risk for renal scarring than older children.⁵ Controversy continues regarding the association of vesicoureteral reflux with the pathogenesis of renal scarring, reflux nephropathy, pyelonephritis and voiding disorders. Although vesicoureteral reflux is associated with renal scarring, its role in the pathogenesis of pyelonephritis and renal scarring is not fully understood. Findings from one study showed that scars formed in 40% of refluxing kidneys and 43% of nonrefluxing kidneys.¹¹

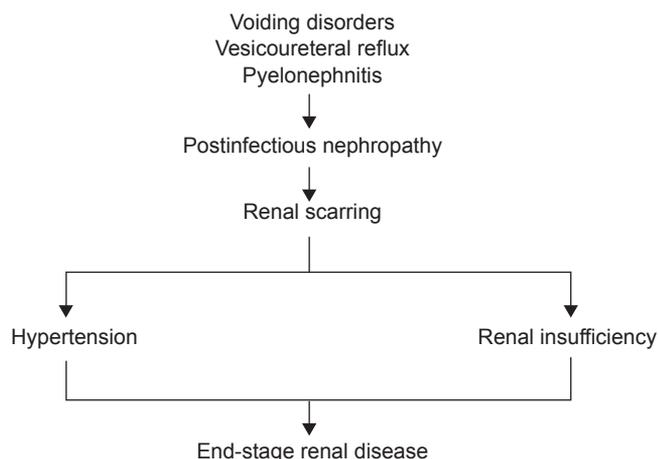


Fig 1: Relationship between urinary tract infection and loss of renal function¹²

Some researchers emphasize the risk of renal scarring from recurrent UTI without reflux. The fact that renal scarring develops in only a minority of patients with pyelonephritis and/or vesicoureteral reflux suggests that the development of renal scarring likely involves the interplay of several factors and cannot simply be attributed to the presence of infection or reflux alone.¹³

Risk Factors

When UTI is diagnosed in a child, an attempt should be made to identify any risk factors for the UTI.⁶ The risk is highest in children having anatomic anomaly, voiding dysfunction, constipation, neurogenic bladder, uninhibited detrusor contraction, girls, and uncircumcised boys. Children who receive broad spectrum antibiotics (e.g., amoxicillin, cephalexin) that are likely to alter gastrointestinal (GI) and periurethral flora are at increased risk for UTI, because these drugs disturb the urinary tract's natural defense against colonization by pathogenic bacteria. Prolonged incubation of bacteria in bladder urine due to incomplete bladder emptying or infrequent voiding compromises an important bladder defense against infection. The rate of UTIs in circumcised boys has been estimated at 0.2-0.4%, with the rate in uncircumcised boys being 5-20 times higher.^{7,8}

Clinical Presentation

The clinical presentation of UTI is variable. In a child with so called 'asymptomatic' bacteriuria, only subtle clues, such as enuresis or squatting, may be present. Alternatively, a systemically ill neonate may be lethargic and hypotensive.³ Although children are often managed on the basis of clinical symptoms and signs alone, these may be unreliable predictors of which patients are at risk for pyelonephritis and scarring.¹⁰ On the other hand, radiologic tests to confirm pyelonephritis or reflux can be expensive, time-consuming, invasive and undesirable to parents and physicians.¹¹

Signs and Symptoms of Urinary Tract Infection in Children⁴:

Urinary tract signs and symptoms

Dysuria

- Frequency
- Dribbling/hesitancy
- Enuresis after successful toilet training
- Malodorous urine
- Hematuria
- Squatting
- Abdominal/suprapubic pain
- Systemic signs and symptoms
 - Fever
 - Vomiting / diarrhea
 - Flank / back pain

The physical examination of a child with a possible UTI should exclude hypertension, an abdominal or flank mass, or a palpable bladder, neurologic deficits, abnormal genitalia and an abnormal urinary stream.⁴ This will help the clinician to find associated disorders. The presence of irritative urinary symptoms in the absence of bacteria suggests a non-UTI cause such as vaginitis, urethritis, pinworms, or the use of bubble baths.⁶

Diagnosis

Maintaining a high index of suspicion for UTI in febrile children, particularly when an unexplained fever lasts two to three days, will lessen the number of missed UTIs. The most recent guideline issued by the American Academy of Pediatrics (AAP) for the evaluation of fever (39.0°C [102.2°F] or higher) of unknown origin suggests urinalysis in all cases and a urine culture in all boys younger than six months of age and all girls younger than two years of age.⁹ In infants, suprapubic aspiration or bladder catheterization and, in older children, a clean voided midstream specimen are essential for diagnosis of UTI.^{3,9} Although convenient, use of adhesive perineal bags or wringing liquid from a wet diaper to collect urine is suboptimal, as bacteria from fecal contamination or urethral colonization may be misinterpreted as UTI.¹⁴ Although there is debate about the best way to screen female infants for UTI,

many support a finding of more than 5 white blood cells per high power field in centrifuged fresh urine is a satisfactory positive screening test.¹⁰

Pyuria, proteinuria and hematuria may occur with or without UTI. Conversely, UTI can occur without pyuria. The determinations of nitrite concentrations and leukocyte esterase are not sensitive enough in children to indicate the need for urine culture.¹⁴

A properly obtained positive urine culture is essential for the diagnosis of UTI.⁹ Any number of colonies from a suprapubic bladder aspiration, more than 10³ colonies from an intermittent catheterization, and more than 10⁵ colonies from a midstream clean catch urine collection indicate UTI. Most UTIs are caused by a single organism; the presence of two or more organisms usually suggests contamination.^{11,14}

Imaging Studies

There is more controversy regarding the appropriateness of different diagnostic imaging modalities in the evaluation of UTI in children.¹¹ The most commonly used imaging techniques are discussed in the following sections.

Ultrasonography

It is used as the initial screening investigation. It is useful in excluding obstructive uropathy and in identifying children with a solitary or ectopic kidney and some patients with moderate renal damage caused by pyelonephritis.¹¹ It is unreliable in detecting vesicoureteral reflux, renal scarring.

A current recommendation is that the following paediatric patients should undergo ultrasonography of the urinary tract after a febrile UTI¹⁵:

- Children with a delayed or unsatisfactory response to treatment of the first febrile UTI.
- Children with an abdominal mass or abnormal voiding (dribbling of urine).
- Children with a first febrile UTI caused by an organism other than *Escherichia coli*.
- Children with recurrence of a febrile UTI after they have had a satisfactory response to treatment of the initial febrile UTI.

Voiding Cystourethrography (VCUG)

VCUG is indicated if renal and bladder ultrasonography reveals hydronephrosis, scarring, or other findings that suggest either high grade VUR or obstructive uropathy. VCUG should be performed if there is a recurrence of a febrile UTI, even if previous ultrasonographic examination findings were unremarkable.¹⁰ Voiding cystourethrography should be delayed until after urinary infection is controlled, because vesicoureteral reflux may be the transient effect of infection.^{11,15} The following types of paediatric patients should undergo VCUG after a first febrile UTI -

- Those in whom treatment fails after 48-72 hours.
- Patients with an abnormal voiding pattern (dribbling of urine).
- Those with an abdominal mass.
- Infants and children with recurrence of a febrile UTI.

Renal Cortical Scintigraphy:

Renal cortical scintigraphy is done for the detection of renal scarring. Renal cortical scintigraphy with either technetium-99m labeled glucoheptonate or dimercaptosuccinic acid (DMSA) are both highly sensitive and specific.¹² DMSA scanning offers the advantages of earlier detection of acute inflammatory changes and permanent scars compared with ultrasound or intravenous urography. It is also useful in neonates and patients with poor renal function.¹⁵

Intravenous Urography:

Intravenous urography appears to have little role in the work-up of UTI in children.¹⁵

Table I: The medical imaging techniques with advantage and disadvantage used in evaluating UTI in children.¹⁰⁻¹⁶

Imaging study	Advantages	Disadvantages
Ultrasound	Measures renal size and shape. Identifies hydronephrosis, structural or anatomic abnormalities and renal calculi. No radiation.	Not reliable to detect vesicoureteral reflux, renal scarring or inflammatory changes. Poor detail in infants.

Voiding cystourethrography	Assesses the size and shape of bladder. Detects and grades vesicoureteral reflux. Evaluates posterior urethral anomalies in boys.	Gonadal radiation. Catheterization.
Renal cortical scintigraphy	Detects pyelonephritis and renal scarring even in early stages. Useful in neonates. Little radiation. Useful in patients with poor renal function.	Does not evaluate collecting system. Cannot detect obstruction.

Treatment

Most cases of uncomplicated UTI respond readily to outpatient antibiotic treatment without further sequelae. Hospitalization is suggested for symptomatic young infants (less than two months of age) and all children with clinical evidence of acute severe pyelonephritis (high fever, toxic appearance, severe flank pain).^{2,4} Initial antibiotic therapy should be based on age, clinical severity, location of infection, presence of structural abnormalities, and allergy to certain antibiotics. Treatment generally begins with a broad spectrum antibiotic, but it may need to be changed based on the results of urine culture and sensitivity testing.¹⁴ Parenteral antibiotics may be used with daily follow up until the patient is afebrile for 24 hours and complete 10-14 days of therapy with an oral antibiotic that is active against the infecting bacteria.¹⁸

Table II: Antibiotic agents for parenteral treatment of a UTI^{17,18}

Drug	Dosage and Route	Comment
Ceftriaxone	50-75 mg/kg/day IV/IM as a single dose or divided q12h.	Do not use in infants <6wk of age; parenteral antibiotic with long half life; may displace bilirubin from albumin.
Cefotaxime	150 mg/kg/day divided IV/IM q6-8h.	Safe to use in infants <6wk of age; used with ampicillin in infants aged 2-8 wk.
Ampicillin	100 mg/kg/day divided IV/IM q8h	Used with gentamicin in neonates <2wk of age; for enterococci and patients allergic to cephalosporins

Drug	Dosage and Route	Comment
Gentamicin	Term neonates <7 days: 3.5-5 mg/kg/dose IV q24h	Monitor blood levels and kidney function if therapy extends >48 h
	Infants and children <5y: 2.5 mg/kg/dose IV q8h or single daily dosing with normal renal function of 5-7.5 mg/kg/dose IV q24h	
	Children =5y: 2-2.5 mg/kg/dose IV q8h or single daily dosing with normal renal function of 5-7.5 mg/kg/dose IV q24h	

Table III: Antibiotic agents for the oral treatment of UTI^{17,18}

Antibacterial Agent	Daily Dosage
Sulfamethoxazole(SMZ) and trimethoprim(TMP)	6-12 mg/kg TMP, 30-60 mg/kg SMZ divided q12h
Amoxicillin and clavulanic acid	20-40 mg/kg divided q8h
Cephalexin	20-50 mg/kg divided q6h
Cefixime	8 mg/kg divided q12-24h
Cefpodoxime	10 mg/kg divided q12h
Nitrofurantoin*	5-7 mg/kg divided q6h

*Nitrofurantoin may be used to treat lower UTIs. However, because of its limited tissue penetration, nitrofurantoin is not suitable for the treatment of kidney infection.

Children with cystitis usually do not require special medical care other than appropriate antibiotic therapy and symptomatic treatment. A 4-day course of an oral antibiotic agent is recommended for the treatment of cystitis. Systematic reviews of treatments for cystitis in children showed no difference in the efficacy of 7-14 days of therapy compared with 2-4 days.¹⁷

Follow up and chemoprophylaxis

A urine culture should be obtained three to seven days after the completion of treatment to exclude relapse. Prophylaxis is recommended for all children younger than five years of age with vesicoureteral reflux or other structural abnormalities and in children who have had three documented UTIs in one year.¹⁸

Table IV: Antibiotic agents to prevent reinfection^{18,19}

Agent	Single Daily Dose
*Nitrofurantoin	1-2 mg/kg PO
Cephalexin	10 mg/kg,
Trimethoprim	1-2 mg/kg PO

* Nitrofurantoin or sulfa drugs are not recommended in infants younger than 6 weeks.

Prevention

A common-sense approach to prevention is advised by most authors. Good hygiene (including 'front-to-back' wiping after urination in girls), avoidance of constipation, circumcision and avoidance of bubble baths, chemical irritants and tight clothing might be recommended.^{2,20}

UTI is a common paediatric problem with the potential to produce long term morbidity. Young children presenting with fever without localizing sign should always be evaluated for UTI.^{1,4,20}

References

1. Quigley R. Diagnosis of urinary tract infections in children. *Curr Opin Pediatr.* 2009; 21(2):194-98.
2. Roberts KB. Urinary Tract Infection: Clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 Months. *Pediatrics.* 2011;128(3):595-610.
3. Pennesi M, L'erario I, Travan L, Ventura A. Managing children under 36 months of age with febrile urinary tract infection: a new approach. *Pediatr Nephrol.* 2012;274(4):611-15.
4. Shaikh N, Morone NE, Lopez J, Chianese J, Sangvai S, D'Amico F, Hoberman A, Wald ER. Does this child have a urinary tract infection? *JAMA.* 2007; 298(24): 2895-904.
5. Lin DS, Huang SH, Lin CC, Tung YC, Huang TT, Chiu NC, Koa HA, Hung HY, Hsu CH, Hsieh WS, Yang DI, Huang FY. Urinary tract infection in febrile infants younger than eight weeks of Age. *Pediatrics.* 2000;105(2):E20.
6. Hoberman A, Chao HP, Keller DM, Hickey R, Davis HW, Ellis D. Prevalence of urinary tract infection in febrile infants. *J Pediatr.* 1993;123(1):17-23.

7. Zorc JJ, Levine DA, Platt SL, Dayan PS, Macias CG, Krief W, Schor J, Bank D, Shaw KN, Kuppermann N. Clinical and demographic factors associated with urinary tract infection in young febrile infants. *Pediatrics*. 2005;116(3):644-80.
8. Zaffanello M, Malerba G, Cataldi L, Antoniazzi F, Franchini M, Monti E, Fanos V. Genetic risk for recurrent urinary tract infections in humans: a systematic review. *J Biomed Biotechnol*. 2010;2010:321082.
9. Lunn A, Holden S, Boswell T, Watson AR. Automated microscopy, dipsticks and the diagnosis of urinary tract infection. *Arch Dis Child*. 2010;95(3):193-97.
10. Andrich MP, Majd M. Diagnostic imaging in the evaluation of the first urinary tract infection in infants and young children. *Pediatrics*. 1992;90:436-41.
11. Mahant S, Friedman J, MacArthur C. Renal ultrasound findings and vesicoureteral reflux in children hospitalised with urinary tract infection. *Arch. Dis. Child*. 2002;86:419-20.
12. Wallin L, Helin I, Bajc M. Follow-up of acute pyelonephritis in children by Tc-99m DMSA scintigraphy: quantitative and qualitative assessment. *Clin. Nuclear Med*. 2001; 26:423-32.
13. Goldraich NP, Goldraich IH. Update on dimercaptosuccinic acid renal scanning in children with urinary tract infection. *Pediatr Nephrol*. 1995;9:221-26.
14. Anad FY. A simple method for selecting urine samples that need culturing. *Ann Saudi Med*. 2001;21(1-2):104-5.
15. Bjorgvinsson E, Majd M, Egli KD. Diagnosis of acute pyelonephritis in children: comparison of sonography and 99m Tc-DMSA scintigraphy. *AJR Am J Roentgenol*. 1991;157:539-43.
16. Keren, R, Chan E. A meta-analysis of randomized, controlled trials comparing short and long course antibiotic therapy for urinary tract infections in children. *Pediatrics*. 2002; 109:70-80.
17. Hoberman A, Wald ER, Hickey RW, Baskin M, Charron M, Majd M, Kearney DH, Reynolds EA, Ruley J, Janosky JE. Oral versus initial intravenous therapy for urinary tract infections in young febrile children. *Pediatrics*. 1999;104(1 Pt 1):79-86.
18. Merguerian PA, Sverrisson EF, Herz DB, McQuiston LT. Urinary tract infections in children: recommendations for antibiotic prophylaxis and evaluation. An evidence-based approach. *Curr Urol Rep*. 2010;11(2):98-108.
19. Hoberman A, Keren R. Antimicrobial prophylaxis for urinary tract infection in children. *N Engl J Med*. 2009;361(18):1804-6.
20. Williams G, Craig JC. Long-term antibiotics for preventing recurrent urinary tract infection in children. *Cochrane Database Syst Rev*. 2011;16(3):CD001534.