

The journal has had 5 points in Ministry of Science and Higher Education parametric evaluation. § 8. 2) and § 12. 1. 2) 22.02.2019.

© The Authors 2020;

This article is published with open access at Licensee Open Journal Systems of Nicolaus Copernicus University in Torun, Poland

Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author (s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non commercial license Share alike. (<http://creativecommons.org/licenses/by-nc-sa/4.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited.

The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 01.06.2020. Revised: 15.06.2020. Accepted: 16.06.2020.

Urinary tract infection in children

Monika Kusz 1, Adam Alzubedi 2, Agnieszka Maślak 1, Paulina Pawluczuk 1,
Paweł Polski 2

1. Department of Paediatric Nephrology, Medical University of Lublin

2. Department of General and Transplant Surgery and Nutritional Treatment,
Medical University of Lublin

Abstract

Urinary tract infections are considered to be one of the most common bacterial infection in children. In 30 % of children with anomalies of urinary tract , urinary tract infection (UTI) can be the first sign. UTIs are classified according to site, symptoms or episode. E. coli is responsible for 80-90 % of acute pyelonephritis episodes. Symptoms include fever, dysuria, tenderness in the lower abdomen are typical for older children, whereas for younger are non-specific. Diagnosis is based on clinical symptoms, abnormal urine analysis and growth on urine culture. Urine culture is still a gold standard for diagnosing urinary tract infections. Antibiotics are usually effective, although antibiotics resistance is still an increasing problem.

Key words: urinary tract infections; bacteriuria; urine analysis

Introduction

A urinary tract infection (UTI) is an infection that affects the kidneys, ureters, bladder or urethra. Kidneys play an essential role in our body, including removing waste products from the body and excess water and maintaining balance electrolyte levels. They also produce erythropoietin, the hormone which stimulates red blood cell synthesis and renin, which regulates blood pressure. Moreover, they take part in converting vitamin D, from the sun to the active form needed by the body. Two ureters drain urine from each kidney into the bladder. Muscles tighten and relax, forcing urine down this tube. The bladder is a small, flexible, triangle-shaped organ in the lower abdomen, which collects and stores urine. The urethra is a thin tube which connects the bladder with the external part of the body.

Epidemiology

UTIs are the most common inpatient and outpatient infections in children. The incidence of UTI in paediatric population is estimated by 2-8%. Acute urinary tract infections are responsible for about 6 % of all medical advice. The prevalence varies with age, with the highest peak in young infants, toddlers and older adolescents. In the adult population, UTIs are responsible for 10-20% of all ambulatory infections and about 40-50 % of hospital infections. There is no similar data for paediatric population.¹ In the neonatal period and the first quarter of life, boys are often exposed to UTIs, which is associated with more frequent congenital anomalies of the urinary tract. After this period, it is observed predominance of female and uncircumcised male infants, even 10-50 times higher risk of UTIs. ¹ Shorter female urethra distance and foreskin surface area in uncircumcised males and are the most important reasons. Moreover, in adolescent females, prevalence peaks again because of sexual activity. Some structural conditions such as urogenital anomalies or functional such as the neurogenic bladder, constipation also increase susceptibility to UTI. More than 30 % of children with UTI will hence recurrent UTI. Vesicoureteral reflux (VUR) or bladder-bowel dysfunction are common risk factors for recurrence UTIs. ²

Classification according to site

Initially, UTIs are categorized based on presentations as uncomplicated or complicated. Uncomplicated typically affects individuals who are healthy with normal functional upper and lower urinary tract with no structural or neurological abnormalities concerning the urinary tract. These infections could be differentiated into lower tract UTIs, which involved infection in the bladder mucosa (cystitis) and urethra (urethritis). The upper UTIs involves infection and diffuse inflammation if the renal parenchyma and pelvis (pyelonephritis) and ureters (Figure 1). Female gender, prior UTI, sexual activity, diabetes, vaginal infections, obesity, genetic susceptibility are considered to be risk factors associated with cystitis. Complicated UTIs are defined as infections, including functional and mechanical obstruction, urinary retention caused by neurological disease, immunosuppression, renal failure, renal transplantation, nephrolithiasis, or indwelling catheters.³

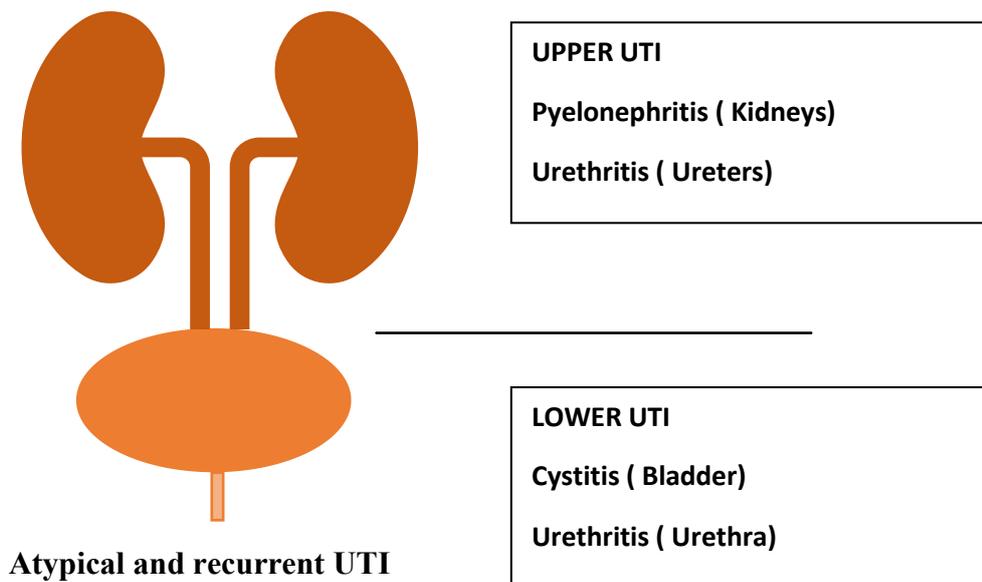


Figure 1. Upper and lower UTI.

Atypical UTI includes seriously ill, poor urine flow, abdominal or bladder mass, raised creatinine, septicaemia, failure to respond to treatment with suitable antibiotics within 48 hours, infection with non-E. coli organisms

Recurrent UTI includes 2 or more episodes of UTI with acute pyelonephritis/upper urinary tract infection, or 1 episode of UTI with acute pyelonephritis/upper urinary tract infection plus one or more episode of UTI with cystitis/lower urinary tract infection, or 3 or more episodes of UTI with cystitis/lower urinary tract infection. ⁴

Symptoms

The clinical presentation of symptoms in children is highly heterogeneous. In older children, the symptoms are often evident. The main symptoms are abdominal and loin pain, urgency during urination, polyuria, or dysuria, fever, anorexia, vomiting, lethargy. In younger patients, especially in newborns and infants, these symptoms are atypical and rarely diagnose accurately. Symptoms of cystitis include frequency, urgency, dysuria, haematuria, or suprapubic pain. The main symptoms of pyelonephritis include fever $\leq 38^{\circ}\text{C}$. ^{5,6}

Etiology

UTIs are caused by both Gram-negative and Gram-positive bacteria as well as fungi. Uropathogenic Escherichia coli (UPEC) is the most common causative agent responsible for 80 % of both uncomplicated and complicated UTIs. For uncomplicated UTIs, the order of prevalence for causative agents, following UPEC as most common is Klebsiella pneumoniae, Staphylococcus saprophyticus, Enterococcus faecalis, group B Streptococcus (GBS), Proteus

mirabilis, Pseudomonas aeruginosa, Staphylococcus aureus, and Candida spp. For the agents involved in complicated UTIs, UPEC is followed in prevalence by Enterococcus spp., K. pneumoniae, Candida spp., S. aureus, P. mirabilis, P. aeruginosa, and GBS.⁷

Pathogenesis

In a physiological condition, the periurethral area has bowel bacteria. In healthy young girls predominates Escherichia coli (E.coli), whereas in boys after the first six months of life, Proteus mirabilis.⁸ Proteus mirabilis, Klebsiella spp., and Staphylococcus saprophyticus are less common.³ UTI may start via hematogenic or ascendant routes. The hematogenic path usually begins in a newborn. A UTI usually starts with periurethral area contamination by a uropathogen living in the gastrointestinal flora, followed by colonization of the urethra and migration to the bladder. It is required appendages such as flagella or pili. Multiple bacterial adhesions recognize receptors on the bladder uroepithelium. Uropathogens such as UPEC can produce toxins and proteases and synthesize siderophores to obtain iron. Consequently, the uropathogenic initiating bacteremia by the ability to cross the tubular epithelial barrier to access the bloodstream. Some uropathogens, including P.mirabilis, S.saprophyticus, K.pneumoniae, and P. aureginosa, encode urease. This enzyme catalyses the hydrolysis of urea to carbon dioxide and ammonia. Consequently, the elevation of urine pH and the production of calcium crystals (apatite) and magnesium ammonium phosphate ammprecipitates (struvite) In urine.⁷

Diagnostic work-up

UTI in children, especially in children below two or three years, may be challenging to diagnose because signs and symptoms in this age group are not obvious.

Medical history

A medical history includes an evaluation of current UTI symptoms, history of urinary tract infections (first episode or recurrent), family health history (especially VUR or renal disease), renal abnormalities, sexual history, constipation. It is also required to ask about diabetes and pregnancy.^{4,9}

Examination

Children with UTI can appear in good condition or very unwell. Tachypnoea, tachycardia or fever may be identified. In physical examination tenderness on palpation or percussion, suprapubic tenderness and flank pain, urine abnormalities such as haematuria, odour, hydration status should be asses.¹⁰

Urinalysis

A urine test should be performed before starting antimicrobial treatment. The recommended method for toilet-trained children is a clean, voided midstream urine sample. However, an APP technical report state that over 85 % of positive culture results obtaining from collecting bag can be false positives.¹¹ For this reason, the sample bag is only reliable when negative. For children who does not control voiding, the four techniques for collecting urine are distinguished. For non-invasive techniques, bags applied to the perineum and clean-catch midstream void (MSU) are included. Before MSU, it is required to wash the skin around the urethra with a soap to reduce contamination. The first part of urine flashes skin flora away from the urethral orifice. MSU has the lowest contamination of all non-invasive methods, is

estimated for about 25 %. Invasive techniques collect urine directly from the bladder by the urethral catheterization or suprapubic needle aspiration (SPA). These methods require specialist equipment to perform and unfortunately, are painful for children. Contamination from catheter and SPA varies from 1 % to 10 %. For this reason, these methods are more predictable for culture.¹² Urine dipstick is a fast and inexpensive test. It provides quick information about nitrate, leukocyte, and microscopic examination for white blood cells (WBC) and bacteria. The presence of nitrate or a positive reaction greater or equal to trace leukocyte esterase causes the urine dipstick positive.¹³ The nitrite dipstick test has high specificity (98%).⁹

Urine culture

Laboratory culture is the gold standard for diagnosing UTI.¹⁴ Urine is placed into a growth medium, where bacteria and antibiotic sensitivities are identified. To diagnose UTI vary on guidelines and collecting methods.

Asymptomatic bacteriuria (ASB) is the presence of bacteria in the urine but without active infection. It occurs between 1,4 to 1,9 % in paediatric population.^{15,16} The traditional definition of clinically significant UTI has been $\geq 10^5$ colonies/ml for clean catch specimen, $\geq 5 \times 10^4$ colonies/ml for catheterized specimens.⁹ The indication for culture include in infants and children who are suspected to have acute pyelonephritis/upper urinary tract infection in infants and children with a high to intermediate risk of serious illness, in infants under 3 months, in infants and children with a positive result for leukocyte esterase or nitrites, in infants and children with recurrent UTI, in infants and children with an infection that does not respond to treatment within 24–48 hours, if no sample has already been sent, when clinical symptoms and dipstick tests do not correlate.⁴

Management

Most children can be treated at home with oral antibiotics and fluids. In contrast, very young children, unwell children with significant urinary tract anomalies and not responding to oral therapy, required admission to the hospital to change treatment to intravenous therapy. Local guidelines conduct the choice of empiric antibiotics. Clinical Excellence (NICE) guidelines propose 7-10 days for pyelonephritis and a three-day course for children > 3 months with cystitis. Infants < 3 months required intravenous antibiotics.⁴ Infants < 3 months required intravenous antibiotics.

Imaging

Ultrasound is a non-invasive tool, an appropriate first-line investigation for UTIs. Ultrasound provides the possibility to detect some anatomical abnormalities, hydronephrosis, megaureter suggesting obstruction, or VUR.

NICE recommends ultrasound only for children less than six months with first UTI unless the infection is atypical or not responding to treatment.⁴

Dimercaptosuccinic acid (DMSA) renal scan

DMSA scan evaluates the size, shape, and position of the kidneys. It is also a useful tool in determining scarring in the kidneys caused by recurrent infections. The drawbacks of this method include radiation exposure (0,3 -3mSV), expensive, and invasive method. Investigations should be conducted after 4 - 6 months after pyelonephritis because only 15 % of children scarring in the kidney could be detected during UTI.^{4, 17} Indications for DMSA scans vary between different guidelines, for instance, Polish guidelines recommend DMSA scans in a patient with VUR III-V, recurrent pyelonephritis.⁹ However, NICE guidelines recommend for children between 6 months and 3 years DMSA 4-6 months after atypical and recurrent infection but for infant more than 3 years or older only with recurrent UTI. ⁴

Voiding cystourethrogram (VCUG)

VCUG is a gold standard to assess bladder urethra, bladder, and urethral abnormalities, including identifying VUR. The main drawbacks of this invasive method are radiation burden, risk of UTI after bladder catheterization, high cost. According to Polish Guidelines, VCUG is performed in children with atypical and recurrent UTIs, febrile UTI, abnormal ultrasound examination, and positive family history for VUR.⁹

Recurrent UTI: prophylaxis and prevention

Prophylaxis should not be performed after the first episode of UTI, without any abnormalities in urinary tract in ultrasound examination, but it should be considered in children with recurrent UTIs and abnormalities in urinary tract.^{4, 9} There is insufficient evidence to support cranberry prophylaxis or probiotics.^{9, 18} Simple hygiene rituals such as wiping front to back in females can avoid entrance bacteria into the urethra. Moreover, avoiding constipation and toilet training is very important to prevent functional bladder bowel dysfunction. ¹⁹

SUMMARY

UTI is common and serious bacterial infection during the childhood. Signs and symptoms are not so typical in young children, however urinary tract infection can be the first sign in 1/3 children with urinary abnormalities. The initial step is to diagnose a treat patients with UTI to prevent recurrent infections, urosepsis or kidney damage

Bibliography

1. Bochniewska V, Jung A, Żuber J. Editorial. 2012;8(1):12-22.
2. Keren R, Shaikh N, Pohl H, et al. Risk factors for recurrent urinary tract infection and renal scarring. *Pediatrics*. 2015;136(1):e13-e21. doi:10.1542/peds.2015-0409
3. Okarska-Napierała M, Wasilewska A, Kuchar E. Urinary tract infection in children: Diagnosis, treatment, imaging – Comparison of current guidelines. *J Pediatr Urol*. 2017;13(6):567-573. doi:10.1016/j.jpuro.2017.07.018

4. Excellence NI for H and C, NICE. Urinary tract infection in under 16s : diagnosis and management. *Nice*. 2018;(August 2007):1-27.
5. Mandracchia VJ, Hayes DW, Yoho RM, Hayes MF. Diagnosis, Differential and Treatment Options. *Nat Rev Microbiol*. 2000;13(March):269-284. doi:10.1038/nrmicro3432.Urinary
6. George NJR. Urinary tract infection. *Sci Basis Urol Second Ed*. 2004:165-203. doi:10.7326/aitc201710030
7. McLellan LK, Hunstad DA. Urinary Tract Infection: Pathogenesis and Outlook. *Trends Mol Med*. 2016;22(11):946-957. doi:10.1016/j.molmed.2016.09.003
8. Kaufman J, Temple-Smith M, Sanci L. Urinary tract infections in children: An overview of diagnosis and management. *BMJ Paediatr Open*. 2019;3(1). doi:10.1136/bmjpo-2019-000487
9. Ekspertów G. Zalecenia Polskiego Towarzystwa Nefrologii Dziecięcej (PTNFD) dotyczące postępowania z dzieckiem z zakażeniem układu moczowego. *Forum Med Rodz*. 2016;10(4):159-178.
10. Escherichia U. Zakażenia układu moczowego (zum) 1.
11. Roberts KB, Downs SM, Finnell SME, et al. 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. doi:10.1542/peds.2011-1330
12. Tosif S, Baker A, Oakley E, Donath S, Babl FE. Contamination rates of different urine collection methods for the diagnosis of urinary tract infections in young children: An observational cohort study. *J Paediatr Child Health*. 2012;48(8):659-664. doi:10.1111/j.1440-1754.2012.02449.x
13. Arakawa S. Urinary tract infections. *Nippon rinsho Japanese J Clin Med*. 2002;60(11):2200-2203.
14. Simões e Silva AC, Oliveira EA, Mak RH. Urinary tract infection in pediatrics: an overview. *J Pediatr (Rio J)*. 2020;96(xx):65-79. doi:10.1016/j.jped.2019.10.006
15. Wettergren B, Jodal U. Spontaneous clearance of asymptomatic bacteriuria in infants. *Acta Paediatr Scand*. 1990;79(3):300-304. doi:10.1111/j.1651-2227.1990.tb11460.x
16. Cain ARR, Furness JA, Selkon JB, Simpson W. Asymptomatic bacteriuria in schoolchildren in Newcastle upon Tyne. *Arch Dis Child*. 1975;50(2):90-102. doi:10.1136/adc.50.2.90
17. Shaikh N, Ewing AL, Bhatnagar S, Hoberman A. Risk of renal scarring in children with a first urinary tract infection: A systematic review. *Pediatrics*. 2010;126(6):1084-1091. doi:10.1542/peds.2010-0685
18. Em S, Am T, Ps L. Probiotics for preventing urinary tract infections in adults and

children (Review) SUMMARY OF FINDINGS FOR THE MAIN COMPARISON.
2015;(12). doi:10.1002/14651858.CD008772.pub2.www.cochranelibrary.com

19. Roberts KB, Downs SM, Finnell SME, et al. Reaffirmation of aap clinical practice guideline: The diagnosis and management of the initial urinary tract infection in febrile infants and young children 2-24 months of age. *Pediatrics*. 2016;138(6). doi:10.1542/peds.2016-3026