

The Clinical Diagnosis of Urinary Tract Infections in Children and Adolescents

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Abstract:

The guidelines of The 2011 American Academy of Pediatrics (AAP) Urinary Tract Infection (UTI): Clinical Practice Guideline for the Diagnosis and Management of the Initial UTI in Febrile Infants and Children 2-24 Months addressed areas for research which identified multiple areas where evidence was lacking. Girls are more likely to be diagnosed with a UTI, outside of the first 12 months. Within the first 12 months of life, about half of boys with UTI will be diagnosed. There are about 85-90% of the cases of UTI is caused by the Escherichia coli which is the most common bacterial pathogens. In this paper, the diagnosis and management of acute and recurrent urinary tract infection in the pediatric and adolescent population is discussed. Related literatures to the urinary tract infections are also summarized in this paper. The prevalence and incidence of pediatric UTI varies by age, sex, race/ethnicity, and circumcision status. Diagnosis of UTI is based on history and exam findings and confirmed with suitably collected urine. There is no need of consent and optimal strategy for imaging in the setting of urinary tract infection in the pediatric population.

Keywords: Urinary Tract Infection, Cystitis, Nephrology, Urology, Paediatrics, Diagnosis

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Introduction

Urinary tract infection is the prevalence of approximately 5% among the children aged of 2-24 months of age and it is the common cause of illness in children. Urine specimens for culture require invasive methods because the presentation of urinary tract infection in children are usually nonspecific and the diagnosis may be clinically challenging. There are many guidelines regarding the goal of guiding clinicians and avoiding delays in diagnosis and treatment have been published over the last few years. American Academy of Pediatrics (AAP), the Subcommittee on Urinary Tract Infection has published the Clinical Practice Guideline for the Initial UTI in Febrile Infants and in Children of 2-24 Months in the year 2011. Technical reports which outlined the current evidences for listed action statements are also complimented along with the publications. The recommendations of a renal and bladder ultrasound (RBUS) for all children after the first urinary tract infection was the most controversial change.

Urinary Tract Infection Morbidity

Urinary tract infection is very common infection in humans mostly in children and adolescents which is caused due to the invasion and replication of the pathogens inside the urinary tract. Nearly 2% of boys and 8% of girls gets affected by the urinary tract infections in the first seven years of life. After otitis media, Urinary tract infection is the second most common bacterial infection in children. The incidence of Urinary tract infection remains on peak in infancy and second peak of the incidence in toddler toilet training years. UTI incidence also increases during the adolescence and it is developed by one in five women during her lifetime. There are about one million patients' clinic visits, over 500,000 emergency department encounters, and 50,000 hospital admissions by the children and adolescents which are diagnosed by the UTI each year in the United States. The number of patients, encounters for the management of UTI has been gradually increased since 2000. 12-30% of children and adolescents who develop a UTI will develop a subsequent infections. Kidney injury, bacteraemia, urosepsis and even death may led by the acute UTI whereas, long term UTI includes hypertension, proteinuria, renal scarring and renal insufficiency.

Pathogenesis of Urinary Tract Infections

The urinary tract is considered as a sterile environment which extends from the urethral meatus to the kidneys and resistant to bacterial colonization. A complete bladder emptying during the urination is the major defense against invading pathogens. Barrier formation

by urothelial cells lining the lower and upper urinary tract, the unidirectional flow of urine, urothelial mucous production, alterations in the urinary ionic composition, and the secretion of antimicrobial peptides and proteins that limit bacterial attachment or directly kill invading uro-pathogens are included in additional innate defences which prevents UTI.

There are about 85-90% of the cases of UTI is caused by the *Escherichia coli* which is the most common bacterial pathogens. The origin of Uropathogenic *E. coli* (UPEC) is thought to be from faecal flora which are spread through the perineum, invades the bladder via urethral opening. In the establishment of UTI, bacterial attachment to the urothelium and internalization is very important. UPEC triggers the host inflammatory response by attaching with the urothelium and by undergoing internalization and resulting in the production of distinct inflammatory mediators. After the inflammatory responses, innate immune cells and proteins activates and migrate to the infectious focus facilitating eradication of the invading bacteria. The results of the inflammatory response is the tissue damage and ultimately UTI.

Clinical presentation of urinary tract infections

Urinary urgency, frequency, dysuria or foul-smelling urine are the characteristics of Cystitis or infection of the lower urinary tract (bladder). Severe or systemic symptoms, including fever, back pain, flank pain or vomiting are generally remains associated with the pyelonephritis, or infection of the upper urinary tract. These symptoms are often absent or difficult to identify in infants and young children. UTI be considered in any infant or child aged between 2 months and 2 years presenting with fever with no identifiable source of infection, recommended by the American Academy of Pediatrics (AAP). Irritability, poor feeding, vomiting or failure to thrive also can be the symptoms along with the fever shown by the infants and young children with UTI whereas, regression to urinary incontinence in previously toilet-trained children, prolonged fever, suprapubic tenderness or significant abdominal pain may be the symptoms in toddlers and young children. Ascending infections may result in bacteraemia in severe situations and present as the systemic inflammatory response syndrome or overt urosepsis. The presence of the systemic inflammatory response syndrome along with the evidence of an infectious aetiology is called urosepsis.

Paediatric Populations at Increased Risk of Urinary Tract Infections

Some of the people have discriminating risk of UTI, however, most of the children and adolescents are subject to UTI. There are few commonly encountered UTI symptoms are tabularized below by the age group.

Table: Commonly Encountered UTI Symptoms

Age group	Common symptoms	Less common symptoms
Newborns, infants	Fever	Vomiting, Irritability, Jaundice, Failure-to-thrive
Young children (not toilet-trained)	Irritability, Abdominal pain , Suprapubic tenderness	Foul-smelling urine, Haematuria
Older children (toilet-trained)	<i>Cystitis:</i> Dysuria, Voiding dysfunction, Incontinence, Frequency <i>Pyelonephritis:</i> Fever, Vomiting, Dysuria, Abdominal or flank pain	Haematuria, Foul-smelling or cloudy urine Malaise

1. Neonates and Infants:

The risk of UTI is at higher level at the few months of life of infants. This susceptibility has been attributed to an incompletely developed adaptive immune system. The incidence of the UTI is greater in boys than the girls under the age of 1 year but after the 1 year, girls are more susceptible to develop UTI than the boys.

2. Circumcision:

The foreskin of the genitals of boys carries increased number of uro-pathogens which can invade the urethral meatus and lead to UTI, therefore, the incidence of UTI in uncircumcised boys increase in the first year of life. According to the policy statement of AAP on circumcision stated in 2012 that, current evidence supports the benefits of circumcision for reducing the risk of UTI and that these benefits justify universal access to the procedure for those who wish it.

3. Constipation and Bowel Dysfunction:

Risk of UTI increases in case of constipation, when the stool bacterial load increases. A stool filled colon may compromise the empty bladder which also increases the risk of UTI. Constipation should be treated immediately as soon as possible because, it recommended by several professional societies to exclude the constipation or bowel dysfunction in the child with UTI.

4. Anatomic and Functional Urinary Tract Anomalies

In children under the 5 years of age, infections that are linked with the abnormalities of urinary tract are noticed. Urine stasis or obstructions can be caused by the Congenital and acquired kidney and urinary tract anomalies (CAKUT) or impaired bladder emptying (i.e. neurogenic bladder) which decreases the clearance of invading pathogens. The urinary tract anomalies may serve as a reservoir for bacterial growth or recurrent infections therefore, it is important to identify urinary tract anomalies early.

5. Spinal Cord Disorders:

The risk of UTI is also increased in the children and adolescents having experience of spinal cord injury or myelomeningocele typically develop neurogenic bladder. Intermittent catheterizations is then performed by these patients and increases risk of UTI when incorrectly performed.

6. Sexual Activity:

The risk of UTI is connected with the sexual activity in female adolescents and young women. This risk is not proven in case of young men.

Diagnosis of UTI

It is the major challenge to diagnose the UTI as it is completely depends upon the method of collecting urine, number of bacterial species cultured and the clinical presentation. Midstream clean catch, catheterization, urine bag or pad, and suprapubic aspiration with or without ultrasound guidance are the methods of urinary collection in children. The controlling power of the urination by the children and level of training and available resources, determines the method of urine collection. A midstream clean catch urine sample is recommended from the children who can control urination, whereas, the choice of technique will depend on the level of training and available resources as well as the patient's clinical status in children who cannot control their urination. If urine is collected by the non-sterile method, the analysis will show the contamination and then this should be repeated using such a technique, which minimizes the risk of contamination. Williams *et al.*,

published the guidelines of the American Academy of Pediatrics for the post test probability of urinary tract infection using dipsticks and microscopy for the diagnosis of UTI. The definite UTI using voided sample is defined by the above guidelines as pure growth of one bacterial species of $\geq 10^8$ colony forming units per liter, a catheter sample of one bacterial species of $\geq 10^7$ colony forming units per liter, or one bacterial species on any amount of urine on a suprapubic aspirate.

The children having complete bilateral urinary tract obstruction or renal tract malformations such as an infected cyst with UTIs and have prior treated, may show the negative result of the urine culture. The UTI causing pathogens in children includes *Escherichia coli* (accounting for over 85% of infections), and rest of the UTI accounts from the *Klebsiella*, *Proteus*, *Enterobacter* and *Enterococcus* species. In such patients following genitourinary surgery and bladder catheterisation and with anatomical defects, organisms seen are *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Group B streptococcus*. Viral infection such as Adenovirus also may cause the UTI generally cystitis.

The presence of bacteria is not required for the diagnosis of UTI, indicated by recent studies and guidelines. Large fraction of fastidious and anaerobic bacteria may be detected by using Polymerase Chain Reaction (PCR), but not detected under culture conditions, it is shown by the Imirzalioglu *et al.* The standard culture conditions used in routine diagnostic laboratories examining urine specimens gets evaded by these groups of bacteria. To uncover these 'hidden' pathogens and during the examination of leukocyte esterase-positive and culture-negative urinary tract specimens, broad-range 16S r-DNA PCR, denaturing high-performance liquid chromatography analysis, sequencing, and bioinformatic analysis is used by this molecular approach.

Review of Literature

Koch and Zuccolotto, (2003) reviewed on urinary tract infection in children and evidence based medicine has taken into consideration. They selected the studies according to their methodology, relevance and clinical applicability. For the diagnosis and treatment of urinary tract infection in children between two months and two years of age, some studies were selected on the basis of parameters proposed by the American Academy of Pediatrics in 1999. Consent statements are still mostly opinion-based on diagnosis and treatment of urinary infection in children and adolescents.

Kwok *et al.*, (2006) investigated the rate of urinary tract infection incidence in Dutch general practice and their association where gender, season and urbanization level was the factor. They also analyzed prescriptions and referral in case of urinary tract infections. They found the incidence rate 8 times higher than the boys and 2 times higher in smaller cities and rural areas than the largest cities. They conclude that the urinary tract infections are not only related to the gender and season but also to the urbanization. Clinical guidelines for urinary tract infections are not followed by the general practitioners in Netherlands especially with respect to referral.

Aiyegoro *et al.*, (2007) studied to identify the incidence of urinary tract infections in children and adolescents and also identified the uro-pathogens which are responsible for the infection and studied the antibiotic sensitivity patterns of the uro-pathogens. They collected clean void urine samples of urine from the children and adolescents of the ages between 5 and 28 years and cultured the samples. They found culture plates with bacterial counts greater than 1×10^5 cfu-ml⁻¹ which is the indication of urinary tract infections. A total of 36 bacterial isolates were obtained among which 28 females and 8 males have the positive urine culture examined.

Okonko *et al.*, (2008) studied the incidence of urinary tract infection among pregnant women in Ibadan, South Western Nigeria. They also isolated and identified the pathogens which are responsible for the infections. The collected samples was 80 clean voided mid-stream urine samples of pregnant women between the ages of 21-40 years. They found 47.5% urinary tract infection among the study population and identified 38 bacteria on the basis of colonial morphology, microscopic characteristics and biochemical tests where the most dominating bacterium was *Escherichia coli* 16. They also found pus cells in 15 of the urine samples which is revealed by the urine microscopy.

Rehman, Ahmed, and Begum, (2014) studied on the occurrence of urinary tract infection in adolescents and adult women of Shanty town in Dhaka city, Bangladesh. They collected urine samples from 462 urinary tract infection suspected females and identified pathogenic bacteria using standard microbiological tests. It is found that the 9% of the subject was possessing the bacteriuria. In adult women aged above 19 years, a higher incidence of urinary tract infection were noted and they suggested regular monitoring of drug resistance phenotype of the urinary tract infection pathogens for reducing the morbidity of females and to offer better treatment strategy in Bangladesh.

Ibeneme *et al.*, (2014) worked on the urinary tract infection in febrile under five children in Enugu, South Eastern Nigeria and attention is paid to UTI as a cause of fever in this age group. They aimed to determine the prevalence of UTI in febrile children with relation to demographic and clinical characteristics and found the prevalence of UTI as 11% and was significantly higher in females than in males. The common clinical features were vomiting, abdominal pain, diarrhea, urinary frequency and urgency. Rate of UTI is higher in the children below 12 years than the 12 years or above 12 years children.

Silva and Oliveira, (2015) discussed recent recommendations for the diagnosis, treatment, prophylaxis and imaging of urinary tract infections in childhood based on evidence. Most common bacterial infection in the childhood is Urinary Tract Infection (UTI) which is found to be more common in boys than the girls. There are so many controversies regarding proper management of the urinary tract infections. They concluded that the proper collection of urine is essential to avoid false positive results during childhood and febrile infants with urinary tract infections should undergo renal and bladder ultrasonography.

Ogbukagu *et al.*, (2016) worked on incidence of urinary tract infections amongst patients attending primary health centers in Anambra State. They determined the prevalence rate of urinary tract infections, age distribution and influence of sex. It is very common disease which are affecting the all age group from neonate to geriatric age group. They found Umunya in southern province have the highest incidence rate of UTI among the towns in Anambra state. Their study provided the evidence of urinary tract infections amongst outpatients of primary health centers and also the drugs for their control.

Chaudhary, Saklani, and Mathuria, (2017) determined the prevalence of urinary tract infections

in children and adolescents of hilly areas of Garhwal region of Uttarakhand, India. They found high prevalence of *Escherichia coli* as the most dominating bacteria which causes the urinary tract infections in children and adolescents. They concluded that their study specifies the incidence of urinary tract infection in children and adolescents. They also highlighted the major bacterial agent involved in that condition of urinary tract infection.

Sarvari *et al.*, (2017) studied the investigation of the relationship between chronic constipation and compare their improvement after the treatment. Urinary tract infection is very common infections caused by the bacteria which can lead to the serious complications such as hypertension, chronic renal failure and renal scar when not diagnosed. They studied on 105 patients having chronic constipation and compared with 104 children without any chronic constipation. After that they compared the prevalence of urinary tract infection in children with and without constipation and also compared their improvement after the treatment.

Conclusion

UTI have the potential to produce long term morbidity and is common problem in children and adolescents. Unclear presenting symptoms, especially in young children is one of the clinical challenges of diagnosing UTI. Therefore, a high index of suspicion is suitable when a young child presents with fever. Antibiotic therapy for febrile UTI should be based on urine culture results and should last for 7-14 days in young children. Renal and Bladder Ultrasound is the appropriate work-up after the UTI in young children and infants. Long term for signs of hypertension and renal insufficiency should be followed by the children with renal scarring an acute UTI.

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