Review Article

Urinary tract infection in children: A narrative review of clinical practice guidelines

Basim S. Alsaywid[1,2], Fahad A. Alyami[1,3,4], Naif Alqarni[1], Khalid Fouda Neel[3,4], Talah O. Almaddah[5], Nada M. Abdulhaq[6], Lujin Bassam Alajmani[5], Mawada O. Hindi[5], Mohammed A. Alshayie[1], Hazim Alsufyani[7], Sarah Abdulrahman Alajlan[2], Bashaer I. Albulushi[1], Safiah K. Labani[8,9]

[1]Department of Urology, King Faisal Specialist Hospital and Research Center, [2]Department of Education and Research Skills Directory, Saudi National Institute of Health, [3]Division of Urology, King Khalid University Hospital, [4]Department of Surgery, Division of Urology, College of Medicine, King Saud University, [8]Research Unit, College of Dentistry, King Saud Bin Abdulaziz University for Health Sciences, [9]King Abdullah International Medical Research Centre, Riyadh, [5]College of Medicine, King Saud Bin Abdulaziz University for Health Sciences, Jeddah, [6]Department of Pediatric, King Abdulaziz University, Rabigh, [7]Department of Surgery, Division of Urology, King Faisal Medical Complex, Taif, Saudi Arabia

Abstract

Background: Urinary tract infection (UTI) has been a major burden on the community and the health-care systems all over the globe. It is the most common cause of bacterial infection in the pediatric age group, with an annual incidence of 3%. The aim of this study is to review and summarize all available guidelines on the diagnosis and management of children with UTI.

Materials and Methods: This is a narrative review of the management of children with a UTI. All biomedical databases were searched, and any guidelines published from 2000 to 2022 were retrieved, reviewed, and evaluated to be included in the summary statements. The sections of the articles were formulated according to the availability of information in the included guidelines.

Results: UTI diagnoses are based on positive urine culture from a specimen of urine obtained through catheterization or suprapubic aspiration, and diagnoses cannot be established on the bases of urine collected from a bag. The criteria for diagnosing UTI are based on the presence of at least 50,000 colony-forming units per milliliter of a uropathogen. Upon confirmation of UTI, the clinician should instruct parents to seek rapid medical assessment (ideally within 48 h) of future febrile disease to ensure that frequent infections can be detected and treated immediately. The choice of therapy depends on several factors, including the age of the child, underlying medical problems, the severity of the disease, the ability to tolerate oral medications, and most importantly local patterns of uropathogens resistance. Initial antibiotic choice of treatment should be according to the sensitivity results or known pathogens patterns with comparable efficacy of oral and parenteral route, for 7 days to 14 days duration. Renal and bladder ultrasonography is the investigation of choice for febrile UTI, and voiding cystourethrography should not be performed routinely unless indicated.

Conclusion: This review summarizes all the recommendations related to UTIs in the pediatric population.

Address for correspondence: Dr. Talah O. Almaddah, College of Medicine, King Saud Bin Abdulaziz for Health Sciences, Jeddah, Saudi Arabia.
E-mail: talah_almaddah@outlook.com

Received: 01.12.2022, **Revised:** 07.02.2023, **Accepted:** 07.02.2023, **Published:** 17.03.2023.

Access this article online	
Quick Response Code:	Website: www.urologyannals.com
	DOI: 10.4103/ua.ua_147_22

How to cite this article: Alsaywid BS, Alyami FA, Alqarni N, Neel KF, Almaddah TO, Abdulhaq NM, *et al*. Urinary tract infection in children: A narrative review of clinical practice guidelines. Urol Ann 2023;15:113-32.

Due to the lack of appropriate data, further high-quality studies are required to improve the level and strength of recommendations in the future.

Keywords: Children, clinical practice guidelines, cystitis, pediatric, pyelonephritis, urinary tract infection, urinary tract infection, vesicoureteric reflux

INTRODUCTION

Urinary tract infection (UTI) is the most common bacterial infection in the pediatric age group in the community and hospital setting, affecting between 3% and 7.5% of febrile children every year.[1] The accumulative incidence of UTIs in children by 6 years of age is 7% for girls and 2% for boys.[2] Children with UTIs have over 1 million annual office visits and 500,000 emergency department visits.[3] Therefore, it has a burden on the child and parents that can lead to short-term complications, such as urosepsis and acute renal failure. UTIs can lead to long-term consequences such as scarring of the kidney, hypertension, and even end-stage renal disease. UTI incidence in pediatrics varies depending on age, race, ethnicity, sex, and circumcision status. The range of incidences reaches significantly high in each gender throughout their 1st year of life during a first-time symptomatic UTI. Boys have a higher incidence than girls in the 1st year of life after which the rate falls, and girls (7.5%) suffer predominantly from UTI, which is 2–4 times higher than boys (2.4%).[1,4-6] The occurrence of UTI is seen in all demographics, with 8% of Hispanic and Caucasian children experiencing it at a rate 2-4 times higher than the 4.7% seen in African American children. The prevalence of UTI in uncircumcised boys (20.1%) is 10 times higher than in circumcised boys (2.4%).[1,5-7] Furthermore, due to nonspecific presentation and unreliable methods for obtaining urine specimens for culture, there are some difficulties in diagnosing UTI in young children. Besides the cost burden of exposing them to unnecessary unpleasant antibiotics, numerous guidelines and reviews were published in recent years with new updates in managing children with UTIs. The following review summarizes an overview of UTIs in children.

MATERIALS AND METHODS

A pragmatic and focused approach was conducted to develop a narrative review and summarize the recommendations of clinical practice guidelines that will impact the practice of Saudi physicians managing pediatric patients with UTIs.

Inclusion and exclusion criteria

Our search included any guidelines covered the diagnosis and management of UTI, where the sample is children, from birth to 18 years old. Moreover, the literature is limited to a complete guideline text published from 2000 to 2022 in high-impact factor journals. Exclusion criteria included any documents that were not original guidelines such as a summary of guidelines or any guideline published before 2000.

Search strategy

PRISMA[8] approach was utilized in our search strategy for screening titles and abstracts and data collection techniques. We conducted a comprehensive and systematic search in January 2022 using the following databases: PubMed, NICE evidence base; Ovid (books; Medline; journals); Embase; Cochrane Library, global health; and gray literature were searched up to December 31, 2021. In addition, searches were conducted in related websites and professional bodies. We used the search terms on all databases: "Guidance," "guideline," "guidelines," "clinical guideline," and "clinical practice guideline."

Study selection

TOA and NMA removed all duplicates and screening titles for relevance. Full-text copies were retrieved and downloaded for screening. The full-text documents were reviewed by LBA and MOH using prespecified inclusion and exclusion criteria. Any discrepancies were resolved by a third reviewer, either BSA or HA. There were 13 documents were included in the conceptualization of the final statements reported in each section of this review. Table 1 summarizes the basic information for all included guidelines in this review.

Data extraction

A data extraction framework was created to draw key characteristics from the guidelines (title, first author name, source of the document, organization, year of publication, and target population). Table 1 summarizes the basic information of all included guidelines in this narrative review. Furthermore, key elements from each guideline were collected in a predetermined data collection sheet addressing different parts of the review from definitions to diagnostic workup and management options. This data collection sheet was piloted by BSA and HA, and amendments were required according to the guideline included. Data were independently extracted by two reviewers: TOA and NMA, from 13 clinical practice

Table 1: Basic information of the included guidelines

	Title	Author name	Source	Organization	Country	Year of publication	Target population
1	UTI: Clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2–24 months	Kenneth Roberts	Pediatrics journal	American Academy of Pediatrics	United State of America	2011	Infants and Children from 2–24 months
2	UTI in children: EAU/ESPU guidelines	Raimund Stein	Journal of European Urology	EAU/ESPU	Europe	2014	Newborn, infants, preschool, school, child, and adolescent
3	UTI s in infants and children: Diagnosis and management	Joan L Robinson	Pediatric Child Health Journal	Canadian Pediatric Society	Canada	2014	Infants and children over 2 months of age with acute UTI
4	Clinical guideline for childhood UTI (second revision)	Seung Joo Lee	Child kidney dis journal	The Korean Society of Pediatric Nephrology	Korea	2015	Neonates, infants, young children, and toilet-trained children
5	KHA-CARI guideline: Diagnosis and treatment of UTI in children	Steven McTaggart	Nephrology Journal	Asian Pacific Society of Nephrology	Australia	2015	Infants and children
6	UTI in children diagnosis, treatment and long-term management	Guideline development group (edited by Andrew Welsh)	NICE	National collaborating center for women's and children's health and NHS	United Kingdom	2007 and updated in 2018	Infants and children
7	Consensus guidelines for the management of pediatric UTI: Northern California pediatric hospital medicine consortium	-	Website: Benioff Children`s Hospitals	Northern California Pediatric Hospital Medicine Consortium	United State of America	2018	All children under age 12 years of age with suspicion or known community-acquired UTI
8	Updated Italian recommendations for the diagnosis, treatment, and follow-up of the first febrile UTI in young children	Anita Ammenti	Acta Pediatrica journal	Italian Society of Pediatric Nephrology and the Italian Society for Pediatric Infectiology	Italy	2019	Infants and young children, 2 months to 3 years of age with first febrile UTI
9	Update of the EAU/ESPU guidelines on UTI in children	Lisette A.Hoen	Journal of Pediatric Urology	EAU/ESPU	Europe	2021	Newborn, infants, preschool, school, child, and adolescent
10	Diagnosis and management of community-acquired UTI in infants and children: Clinical guidelines endorsed by the SPIDS	May Albarrak	International Journal of Pediatrics and Adolescent Medicine	King Faisal Specialist Hospital and Research Centre	Saudi Arabia	2021	Pediatric age group from 3 months of age up to 14 years with uncomplicated
11	Asian guidelines for UTI in children	Steph S.Yang	Journal of Infection and Chemotherapy	Japanese Society of Chemotherapy and the Japanese Association for Infectious Diseases	Taiwan, Republic of Korea and Japan	2021	Infants and children (no specific age)
12	Swiss consensus recommendation on UTI in children	Michael Buettcher	European Journal of Pediatrics		Switzerland	2021	Children with Suspected or recurrent UTI. Neonate up to 16 years of age
13	UTI in under 16s: Diagnosis and management	-	NICE	-	UK	2022	Babies and children from birth up to the age of 16 years with UTI, their families and carers

SPIDS: Saudi Pediatric Infection Diseases Society, NICE: National Institute for Health and Care Excellence, EAU: European Association of Urology, ESPU: European Society of Pediatric Urology, UTI: Urinary tract infection, KHA-CARI: Kidney Health Australia-Caring for Australasians with Renal Impairment

guidelines and disagreements were resolved by discussion. The final statement in each subsection of this review was drawn from those 13 guidelines. Table 2 summarizes the recommendations statements from all included guidelines and displays the variation of practice.

RESULTS

Definitions and classification

Infection of the urinary tract is an inflammatory response of the urothelium to bacterial invasion that is usually

Table 2: Summary recommendations from all included guidelines

Title	Definition	Risk factors	Clinical presentation	Methods of urine specimen collection	Other laboratory test	Management	Imaging studies	Admission criteria	Prevention
1	To establish the diagnosis of UTI, clinicians should require both urinalysis results that suggest pyuria and/or bacteriuria and the present of at least 50,000 (CFUs/mL) of uropathogen cultured from urine specimen obtained through catheterization or SPA		If a clinical assesses a febrile infant with no apparent source for the fever as not being so ill as to require immediate antimicrobial therapy, then the clinician should assess the likelihood of UTI if low likelihood then clinical follow up is sufficient If the infant not in a low-risk ether to collect urine by SPA and catheterization for UA and culture, or to collect urine for. UA and if turned out positive collect other ample by SPA or catheterization	Febrile infant with no apparent source for the fever requires antimicrobial therapy after obtaining urine specimen for both culture and urinalysis; the specimen needs to be obtained through catheterization or SPA, because the diagnosis of UTI cannot be established through culture of urine collected in a bag		When initiating treatment, the clinicians should base the choice of route; orally or parenterally both equally effective. The clinician should base the choice of agent on local antimicrobial sensitivity patterns and adjust according to sensitivity testing of the isolated uropathogen The duration should be between 7 and 14 days	Febrile infants with UTI should undergo RBUS VCUG should not be performed routinely after the first febrile UTI; VCUG is indicated if RBUS reveals hydronephrosis, scarring, high-grade VUR, or obstructive uropathy as well as atypical or complex circumstances		
2	For urine specimen from suprapubic bladder puncture; any number of CFU/mL Bladder catheterization >1000–50,000 CFU/mL Midstream no I'd >10^4 CFU/mL with symptom >10^5 CFU/mL		Neonate can percent with nonspecific symptoms (failure to thrive, jaundice, vomiting, hyperexcitability, lethargy, hypothermia, with or without fever In older children, lower urinary tract symptoms include dysuria, stranguria, frequency, urgency, incontinence, hematuria, and suprapubic pain And for the upper urinary tract fever and flank pain	Newborn, infants and nontoilet-trained children: A plastic bag if positive further clean catch or SPA or cather action to further confirm the diagnosis Toilet-trained children, CV midstream	Serum electrolytes and blood cell counts should be obtained for monitoring ill patient Creatinine CRP Procalcitonin	In febrile children with signs of UTI, antibiotic should be initiated as soon as possible Parental antibiotic is recommended in newborns and infant < 2 months Antibiotic should be given for 7–14 days	<1 year of age, exclusion of VUR >1 year of age girl exclusion of VUR >1 year of age boy; exclusion of VUR after recurrent febrile UTIs Toilet trained girl specific; exclusion of LUTS/BBD Toilet trained boy specific; exclusion of LUTS/BBD, exclusion of VUR f there is a suspicion		Prophylaxis antibiotics should be considered in cases of high susceptibility to UTI and risk-acquired renal damage Cranberry juice
3		Fever > 39 with no apparent source, age < 12 months, white race, temperature > 39		Not toilet-trained: Urethral catheterization Bag specimen is used initial screen and subsequent specimen is obtained	Blood cultures need not be performed unless the child is hemodynamically unstable Renal function should be monitoring	Oral antibiotic should be between 10 and 14 days while IV for 3 days followed by 10 days oral	In case of complicated UTI a RBUS is recommended to look for obstruction and children <2 years		Antibiotic prophylaxis pending results of imaging is no longer advised routinely

Contd...

Table 2: Contd...

Title	Definition	Risk factors	Clinical presentation	Methods of urine specimen collection	Other laboratory test	Management	Imaging studies	Admission criteria	Prevention
				by Catheterization or SPA For toilet-trained children, a mid-stream urine should be collected by CVU	has a complicated UTI		of age with first febrile UTI VCUG was recommended routinely for children between 2 months and 2 years but not anymore		
4	Positive urine culture in the SPA and TUC urine. When a urine culture is positive (>10^5 CFU/mL) in SBC urine. UTI should be diagnosed only in children with both definite symptoms and abnormal urinalysis	Females First UTI commonly devolved in male infants, who are uncircumcised	High fever, flank pain, vomiting for pyelonephritis, dysuria, voiding dysfunction, turbid urine, suprapubic pain for cystitis Infants and children with toxic usually experience vomiting, poor feeding, dehydration, lethargy, or weak cry	The ideal methods for urine collection: SPA or TUC in nontoilet-trained children who are very ill. SBC fist in these who are not so ill and then SPA or TUC if urinalysis is abnormal		Febrile UTI children <3 months, toxic or unable to retain oral intake should receive antibiotic parenterally. Oral antibiotic as effective as the combination of oral and parenteral. The minimal duration 7 days	DMSA is a gold standard to diagnose pyelonephritis and renal scar VCUG is not routinely recommended RBUS is useful to detect urinary abnormalities and renal infections		Antibiotic prophylaxis is not recommended any more in children without or with VUR (Grade I–IV) For physiologic phimosis, topical steroids for 2–4 weeks will be a first-line treatment. Rather than neonatal circumcision Cranberry is a natural food to prevent recurrent UTI
5	Diagnosis of UTI only made by clinical symptoms in association with positive urine culture SPA: Any growth CSU: >108 CFU/L MSU or CCU >108			Culture is recommended by the urine collected specimen Clean catch is recommended, mid-stream urine, or in-out catheter specimen If positive culture was obtained by bag, its recommended to repeat the culture by SPA, CSU, CCU, MSU		If the positive urine culture and absent of clinical symptoms does not warrant treatment or further investigation for UTI Recommended to start treatment for presumed UTI in children who have clinical symptoms suggestive of UTI and who have positive leukocyte or nitrate on urinary dipstick or microscopy The optimal duration is unknown, but	Routine renal tract imaging following first UTI is not recommended except children <3 months, have a urine culture with atypical organism, concurrent bacteremia renal impairment, abdominal mass or poor urinary stream MCUG is recommended if VUR is suspected And prophylactic	In children who are younger than 1 month of age or children older than 1 month who appear septic, dehydrate or unable to retain oral intake, initial anti-microbial therapy	Routine circumcision for boys after first UTI is not recommended only for boys with recurrent UTI or hi-grade fever Cranberry concentrate is recommended not to be used for UTI prevention Avoidance of constipation, increase fluid intake, avoiding bubble bath

Contd...

Table 2: Contd...

Title	Definition	Risk factors	Clinical presentation	Methods of urine specimen collection	Other laboratory test	Management	Imaging studies	Admission criteria	Prevention
						7–10 days is currently recommended	antibiotics should be given at the time of MCUG DMSA is not recommended in the acute phase		
6	A UTI is defined by a combination of clinical features and the present of bacteria in the urine		Unexplained. Fever of 38° C Most common symptom in infants <3 months; fever, vomiting, lethargy, irritability And in infant and children 3 months or more; fever, frequency, dysuria	A clean catch urine sample is the recommended method for urine collection. If a clean catch urine sample is unobtainable: Other noninvasive methods such as urine collection pads should be used In infants and children When it is not possible or practical to collect urine by noninvasive methods, catheter Sam-plus, or SPA should be used		Infants younger than 3 months with a possible UTI should be referred immediately to the care of a pediatric specialist. Treatment should be with IV antibiotics For infants and children 3 months or older Treat with oral antibiotics for 7–10 days. The use of an oral antibiotic with low resistance patterns is recommended If oral antibiotics cannot be used, treat with an IV antibiotic agent	I ultrasound during acute infections only recommended to atypical UTI infants and children Ultrasound within 6 weeks recommended for infants and children with UTI DMSA 4–6 months following the acute attack recommended to infant with a typical UTI and recurrent UTI infants and children MCUG not recommended to infant and children		Antibiotic prophylaxis should not be routinely used in children and infants following first-time UTI Drink adequate amount of fluid Have an access to clean toilets Antibiotic prophylaxis may consider in infants and children with recurrent UTI
7	A combination of clinical symptoms, pyuria, and positive urine culture with > 50,000 CFU/mL	Recurrent UTIs, GU anomaly, high-grade VUR, recent catheterization, recent GU instrumentation	Nonspecific: Fever without source, abdominal pain, vomiting without diarrhea, focal symptoms: Dysuria, flank pain, suprapubic tenderness	Infants <6 months: catheter for UA and culture Children >6 months: Clean catch for UA and culture Children > 6-month nontoilet-trained: Send bag or catheter specimen for UA Bag specimen not be sent to culture	Blood culture for febrile infants < 3 months LP: All febrile neonates Metabolic panel, electrolyzes, lactate, CBC, or CRP not routinely recommended	Antibiotics recommended in children < 3 months with positive UA 3 months–1 year is febrile with positive UA Any child with positive UA who is toxic-appearing 3 months–12 years who are a febrile and well-appearing with holding empiric treatment till the result	Renal and bladder ultrasound: Sever clinical course, recurrent UTI, complicated UTI in children <2 years, infants <6 months of age with first febrile UTI VCUG: not routinely recommended after first UTI DMSA: Not routinely recommended in evaluation of UTI	Clinically ill Severe dehydration Neonates with fever Positive blood culture Urine culture positive for multi-drug resistant Unable to tolerate oral medication Failure to respond to outpatient therapy	

Contd...

Table 2: Contd...

Title	Definition	Risk factors	Clinical presentation	Methods of urine specimen collection	Other laboratory test	Management	Imaging studies	Admission criteria	Prevention
8	SPA: Any growth Transurethral BC: 50,000 CFU/mL CVU: >100,000 CFU/mL Bag: >100,000	Pathogen other than *E. coli* Abnormal RBUS Abnormal prenatal ultrasound Male younger than 6 months at UTI attack	2–3 months: Lethargy, irritability, fever, and vomiting In older children: Frequency, dysuria, abdominal pain, loin tenderness, and fever	Initially UA if abnormal urine culture Bag not recommended CVU recommended in primary care centers Transurethral sample in hospital sitting or circul ill patients SPA gold stander but not feasible	Blood test is not necessary, but recommended in infants < 3 months	In a febrile child unwell appearing, <3 months, severely ill, persisting fever, or low compliance: Start IV treatment switch to oral as soon as the clinical condition allow Febrile + well appearing: Oral route Treatment should be between oral 10 and 14 days Or IV	RBUS: All children 2–4 weeks after the first febrile UTI Scintigraphy is not routinely recommended VCUG is recommended after fist UTI or abnormal RBUS or if the bacterial organism other that *E. coli*		Circumcision is conceivable is recommended in selective cases Antibiotic prophylaxis: Not routinely recommended after the first febrile UTI. It may be considers in children with reflux Grade IV and V
9	Classifications		Nonspecific symptoms such fever, lethargy, vomiting and failure to thrive	In neonate, infants and nontoilet-trained: Plastic bag, CCU, transurethral bladder catheter, or SPA It is recommended to use two-step procedure which may lead to less invasive procedure In toilet-trained children; clean catch, I dream		The choice between oral or parental therapy should be based on patient age; clinical suspicion of urosepsis; illness severity; refusal of fluid; noncompliance Treatment febrile UTI with 4–7 days course of oral or parental therapy	Renal and bladder ultrasound within 24 h is advised in infant with febrile UTI to exclude obstruction VCUG is the gold standers diagnostic test for VUR is VCUG		Long-term antibacterial prophylaxis in case of high susceptibility to UTI and risk of acquired renal damage and lower urinary symptoms
10	Significant bacteriuria of a urinary pathogen in a symptomatic patient SPA: Any number of CFUs/mL Catheter: 50,000 CFUs/mL Clean catch: >100,000 CFU/mL	Female > male Febrile female <12 months uncircumcised male infant with fever children with obstructive urological abnormalities VUR BBD	In infant: Fever, irritability, lethargy, poor feeding or GI symptom In older children: Fever, urinary symptom, vomiting, abdominal pain, or suprapubic tenderness	For neonates: SPA for infant: Transurethral BC For toilet-trained: CVS Against the use of sterile urinary bag	CBC, inflammatory markers, serum creatinine, blood culture or LP Not routinely obtained in infant older that 3 months who appear healthy	Febrile + urinary symptom: Start empiric antibiotic for UTI while waiting for urine culture result Afebrile + urinary symptom: Check dipstick if positive start empiric antibiotic If negative wait for urine culture	RBUS and VCUG is recommended in first febrile UTI in <3 years old, recurrent UTI, complicated UTI, or Hx of VUR RBUS should be performed between 2 and 6 weeks where VCUG last days of antimicrobial therapy DMSA is only recommended in impaired renal function or UTI with severe VUR		Antibiotic prophylaxis is recommended for Moderate to high-grade reflux Uncircumcised males with VUR Children with BBD and VUR Nitrofurantoin: 1–2 mg/kg/day Trimethoprim/sulfamethoxazole: 2 mg/kg/day

Contd...

Table 2: Contd...

Title	Definition	Risk factors	Clinical presentation	Methods of urine specimen collection	Other laboratory test	Management	Imaging studies	Admission criteria	Prevention
							between 4 and 6 months		
11	The cutoff for defining UTI by catheterization is always considered 10,000 CFU/mL	Labia adhesion, BBD, phimosis, vaginal reflux, short VA distance Diaper; entrance of bacteria BBD, neurogenic bladder, anatomical BOO; retention and multiplication of bacteria in UB BBD, young age, short tunnel Hutch's, diverticulum; VUR	Your female children with UTI present with nonspecific symptom; fever, sepsis, lethargy, prolonged jaundice, hematuria, poor feeding, vomiting diarrhea, abdominal pain, irritability, failure to thrive, cloudy malodorous urine In older children; the symptoms and sign are more specific; fever, chill mess, vomiting, back and abdominal pain, lower urinary tract symptoms Include suprapubic pain, dysuria, urinary frequency, urgency, day wetting and cloudy urine	Urine culture is gold standard SPA or TUC are strongly recommended For toilet-trained children, urine specimens for culture can be obtained by midstream Plastic bag not recommended For nontoilet-trained; bag specimen can be used initial urinalysis subsequent culture is obtained by cauterization or SPA In young children, urine is usually collected by catheterization or SPA		Oral antibiotics cab be used effectively on an outpatient >3 months of age <3 months it is recommended initial hospitalization and parental antibiotic after complete septic workup Or severely ill children immunocompromised, intolerance to oral intake, urinary tract	Imaging studies are done to identify risk factors RBUS serve an ideal for initial screening for anatomical abnormalities on infant because it's noninvasive DMSA is gold standard for identifying acute pyelonephritis or renal scarring It is preferred for infants with febrile UTI VCUG is the gold-slandered classifying grade of VUR Can detect bladder dysfunction, posterior urethras valves, ureterocele, utricle cyst or neurogenic bladder		Significant urinary tract obstruction Trimethoprim or cotrimoxazole and nitrofurantoin have been substances mostly used
12	A positive urine culture in urine obtained by catheterization, the growth of a single uropathogen >10,000 CFU/mL and in MSU sample, the growth of a single uropathogen >100,000 are highly suggestive of UTI	Congenital anomalies of kidney or urinary tract Family history of VUR or renal disease Uncircumcised male infant Abnormal urine flow or dysfunctional voiding Constipation	In neonates and infants; fever, poor feeding, failure to thrive, lethargy, irritability, pyuria, bacteriuria	In infants and toddlers, bladder catheterization and SPA are recommended methods of urine collection and are considered the gold standard	In case of parental therapy is indicated, blood culture should always be obtained In neonates, a sepsis workup	Treatment of UTI (choice of antimicrobial, route of administration) should be based on age and clinical presentation, as well as risk factors from the patient's past medical history. In children <60 days, consider always starting with parenteral treatment. In children >60 days in	All children, regardless of age, should have an ultrasound of the urinary tract performed after the first episode of pyelonephritis Micturition cystourethrogram should only be planned under certain circumstances		In general antibiotic prophylaxis is not recommended

Contd...

Table 2: Contd...

Title	Definition	Risk factors	Clinical presentation	Methods of urine specimen collection	Other laboratory test	Management	Imaging studies	Admission criteria	Prevention
		History suggesting previous UTI or confirmed recurrent UTI				good general condition initiating treatment orally or parenterally is equally efficacious (evidence quality: High recommendation: strong). Local antimicrobial sensitivity patterns (if available) should be considered when choosing an empirical agent. Adjustment of the initial treatment should be done according to AST of the isolated uropathogen (evidence quality: High recommendation: Strong). The clinician should choose 7–10 days as the total duration of antimicrobial therapy for upper UTI			
13			Unexplained fever of 38 C or higher Infant <3 months; most common to least common; fever, vomiting, lethargy, irritability, poor feeding, failure to thrive, abdominal pain, jaundice, hematuria, offensive urine Infant and children >3 months Fever, frequency, dysuria Loin tenderness Dysfunctional voiding	A clean catch urine sample is the recommended methods for urine if clean catch unobtainable urine collection pads When it is not possible or practical to collect by noninvasive, catheter sample or SPA should be used Before SPA is attempted ultrasound guidance should be used to demonstrate	CRP should not be used to differentiate acute pyelonephritis/ upper UTI from cystitis/lower UTI in infants and children	Infants <3 months with possible UTI should receive parenteral antibiotics For infants and children >3 months or older with acute pyelonephritis/upper UTI Should be treated with antibiotics As well as asymptomatic bacteriuria	Infants and children with atypical UTI should have ultrasound of the urinary tract For infants <6 months with first time UTI, ultrasound should be carried out within 6 weeks of the UTI A DMSA scan 4–6 months following the acute infection Routine imaging to identify VUR is not		Drink an adequate amount of fluid Should have ready access to clean toilets when required and should not be expected to delay voiding Antibiotic prophylaxis should NOT be routinely recommended in in infant ad children following first-time UTI

Contd...

Table 2: Contd...

Title	Definition	Risk factors	Clinical presentation	Methods of urine specimen collection	Other laboratory test	Management	Imaging studies	Admission criteria	Prevention
				the presence of urine in the bladder			recommended, except in specific circumstances		

1. UTI: Clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2–24 months, 2. UTI in children: EAU/ESPU guidelines, 3. UTI s in infants and children: Diagnosis and management, 4. Clinical guideline for childhood UTI (second revision), 5. KHA-CARI guideline: Diagnosis and treatment of UTI in children, 6. UTI in children diagnosis, treatment, and long-term management, 7. Consensus guidelines for management of pediatric UTI: Northern California Pediatric Hospital Medicine Consortium, 8. Updated Italian recommendations for the diagnosis, treatment, and follow-up of the first febrile UTI in young children, 9. Update of the EAU/ESPU guidelines on UTI in children, 10. Diagnosis and management of community-acquired UTI in infants and children: Clinical guidelines endorsed by the SPIDS, 11. Asian guidelines for UTI in children, 12. Swiss consensus recommendation on UTI in children, 13. UTI in under 16 s: Diagnosis and management. KHA-CARI: Kidney Health Australia-Caring for Australasians with Renal Impairment, EAU: European Association of Urology, ESPU: European Society of Pediatric Urology, SPA: Suprapubic aspiration, TUC: Transurethral catheterization, SBC: Sterile bag collection, CSU: Catheter specimens of urine, MSU: Midstream urine, CCU: Clean-catch urine, BC: Bladder catheterization, CVU: Clinical vaccinology update, UTI: Urinary tract infection, GU: Genitourinary, VUR: Vesicoureteric reflux, *E. coli: Escherichia coli*, RBUS: Renal and bladder ultrasonography, BBD: Bowel and bladder dysfunction, UB: Ureolytic bacteria, CRP: C-reactive protein, CBC: Complete blood count, LP: Lumbar puncture, IV: Intravenous, AST: Antimicrobial sensitivity testing, VCUG: Voiding cystourethrography, DMSA: Dimercapto succinic acid, MCUG: Micturating cystourethrogram, CV: Clean void, CCS: Clean catch sample, CFUs: Colony-forming units, VA: Vaginoanal or anovaginal, BOO: Bladder outlet obstruction

associated with a group of clinical presentations, pyuria, and positive urine culture with >50,000 colony-forming unit (CFU)/ml of a single pathogen on a properly collected culture.

Bacteriuria can be asymptomatic which indicates the isolation of a specified quantitative number of bacteria in an appropriate collection from an individual's urine specimen without the presence of symptoms or signs of UTI. While symptomatic bacteriuria consists of positive culture with the presence of symptoms such as lower urinary tract symptoms (storage or voiding), suprapubic pain, fever, hematuria, flank pain, and malaise (pyelonephritis). In patients with a neurogenic bladder and malodorous urine, it is hard to differentiate among asymptomatic and symptomatic bacteriuria. Correspondingly, infection is often defined clinically by their presumed site of origin. Upper urinary tract (pyelonephritis) is a diffuse pyogenic infection of the renal pelvis and parenchyma. Symptoms include fever over 38°C, while infants and young children are associated with nonspecific signs such as poor appetite, failure to thrive, lethargy, irritability, vomiting, or diarrhea, whereas lower UTI (cystitis) is an inflammation of the mucosa of the urinary bladder. Symptoms include dysuria, stranguria, frequency, urgency, urine malodor, incontinence, hematuria, and suprapubic pain. However, these symptoms are rarely accurately diagnosed in newborns and infants.

UTIs may also be described in terms of the urinary tract's anatomical or functional status and the host's health. Uncomplicated UTI is an infection in a patient with a normal morphological and functional upper and lower urinary tract, normal renal function, and a competent immune system. Complicated UTIs occur in children with known mechanical or functional obstructions or upper and lower urinary tract problems.

UTIs can also be defined by their relationship to other UTIs; a first or isolated infection occurs in an individual who has never had a UTI or has a remote UTI infection from a previous UTI. An unresolved infection is one that has not responded to antimicrobial therapy and is documented as having a similar resistance profile with the same organism. Recurrent infection is one that occurs after an antecedent infection has been documented as successfully resolved. Consider these two recurrent types of infection: Reinfection describes a new event involving the reintroduction of bacteria from outside into the urinary tract. Persistence refers to a recurrent UTI caused by the same urinary tract-directed bacteria, such as an infectious stone or a prostate.

Community-acquired UTIs occur in patients who at the time of infection are not hospitalized or institutionalized. Infections are usually caused by common bacteria in the intestine (e.g. *Enterobacteriaceae* or *Enterococcus faecalis*) that are susceptible to most antimicrobials. Nosocomial or health-related UTIs occur in hospitalized or institutionalized patients, typically caused by *Escherichia coli* or *Pseudomonas* and other strains that are more antimicrobial-resistant.

These definitions and types require a careful clinical and bacteriological evaluation and are important because they affect the type and extent of the evaluation and treatment of the patient.[9]

Pathogenesis

UTIs are the result of the interactions between uropathogen and host. It occurs when uropathogens climb through the urinary tract from periurethral colonization to the bladder or invade the bloodstream. Rarely, a hematogenic and direct invasion occurred. All possible routes for transmission are catheterization, voiding patterns, sexual intercourse, or genital manipulation. UTI is determined by bacterial virulence, anatomical variance (gender, vesicoureteral reflux [VUR], and circumcision), bowel and bladder dysfunction resulting in urinary stasis (constipation and neurogenic bladder), and host defenses (periurethral and gastrointestinal tract genetics and flora), these factors affect the colonization level and damage the urinary tract.[4] Children's risk factors for UTI are summarized in Box 1.

Pathogen (microorganism)

The most common cause of UTIs is *E. coli*, accounting for 85% of community-acquired infections and 50% of hospital-acquired infections.[9] Other Gram-negative organisms responsible for most community-acquired infections include *Enterobacteriaceae*, including Proteus and *Klebsiella*, in addition to Gram-positive *E. faecalis* and *Staphylococcus saprophyticus*. While nosocomial infections are caused by *E. coli*, *Klebsiella*, *Enterobacter*, *Citrobacter*, *Serratia*, *Pseudomonas aeruginosa*, *Providencia*, *E. faecalis*, and *Staphylococcus epidermidis*.[9]

Box 1: Risk factors for urinary tract infection in children

Abnormal voiding, dysfunctional elimination and/or constipation
Previous history of UTI
Fever of unknown origin
Antenatally diagnosed renal abnormalities or evidence of spinal lesion
Family history of VUR or renal disease
Uncircumcised boys (1st year of life)
Anatomical abnormalities (pelviureteric junction obstruction, VUR, ureterovesical junction obstruction)

UTI: Urinary tract infection, VUR: Vesicoureteric reflux

Fungal UTIs such as infections with *Candida albicans* often overlap with recent antibiotic therapy, urinary catheterization, or immunosuppression. Adenoviruses are known to cause hemorrhagic cystitis. However, the BK virus (polyomavirus) is an immunosuppression-associated causative organism.[4]

CLINICAL MANIFESTATIONS

The presentation of children with UTI should be promptly evaluated. To prevent further complications, early recognition and treatment of UTI are important factors. Classification of the clinical presentation for UTI is based on estimated age ranges consisting of (a) neonate, from birth to 2 months of age; (b) infancy, between 2 months and 2 years of age; and (c) children more than 2 years of age. UTI is nonspecific in infants and young children and is more evident as the child grows older. UTI should, therefore, be suspected in any febrile infant until it is confirmed, as it can induce complications such as urosepsis and renal scarring. The site, episode, symptoms, and complicating factors are recognized by taking the patient's history, which includes questions about primary or recurrent infection, febrile or nonfebrile UTIs, and urinary tract malformation (pre- and/or postnatal ultrasound [US] findings). In addition to a family history of urological abnormalities, particularly VUR, previous surgery, drinking, and voiding habit. Other relevant history includes bowel habits (history of constipation), amount of fluid intake, the presence of lower urinary tract symptoms, and sexual history in teenagers.[10] Table 3 highlights the range of features found in UTI cases in children of different age groups.

Although there is no pathognomonic sign for a UTI, fever may be the only symptom and sign of UTI, especially in young children. Therefore, physical examination is necessary to exclude any other source of fever, especially if there is no clear cause for fever. Physical examination should evaluate whether the patient is sick or well, evaluate the hydration status, along with examining the abdomen to exclude any palpable kidney or bladder, external genitals to exclude any genital disorder, and lower limbs. Conditions such as spina bifida, phimosis, labial adhesions, or sexual abuse signs may be presented.[4]

Sexual abuse of children affects 10%–40% of girls and 5%–20% of boys. Girls are abused more often than boys, but boy abuse is more often associated with physical violence. Children are referred to a urologist due to urogenital complaints such as recurrent infection, hematuria, dysuria, chronic lower abdominal pain, daytime urinary retention,

and nighttime incontinence, or symptoms such as lower urinary tract symptoms (LUTS): Nocturia, urinary frequency, painful voiding, or urgency. Diagnosis of child sexual abuse is only possible through proper medical history collection and physical examination. As a result, the high authority center should be notified of any suspicion of sexual abuse cases.

INVESTIGATIONS

Urine collection

Urine collection should be obtained if unexplained fever is higher than 38°C, and UTI features are suspected before using any antibacterial agents. Sampling of urine in infants will be challenging and should be done using one of these methods; Table 4, noninvasive techniques include a sterile bag applied to the perineum sterile bag collection (SBC) and clean catch midstream void, whereas invasive methods include transurethral catheterization (TUC) and suprapubic aspiration (SPA).[4]

Table 3: Clinical features of urinary tract infection in children

Age group	Common	Less common
Neonate (birth–2 months)	Fever	Poor feeding, vomiting
Infancy (2 months–2 years)	Irritability	Hematuria Foul smelling urine, cloudy urine
Children (>2 years)	Pyelonephritis: High fever Vomiting Loin pain	Abdominal pain Malaise
	Cystitis: Dysuria Lower urinary symptoms	Hematuria Foul smelling urine, cloudy urine

Appropriate urine collection should complete the UTI diagnosis. The technique used to obtain urine will affect the rate of contamination and in turn affect the interpretation of the results. Since each method has its advantage and disadvantage, the best way to select is according to age, the severity of symptoms, and toilet-training status.

Clean midstream catch (CMC) is the method of choice for the diagnosis of UTI in toilet-trained children, the midstream urine is collected twice. SPA is a gold standard method in nontoilet-trained children with unexplained fever or sepsis. The success rate is very high, although it is invasive but rarely complicated. TUC is a less invasive method but more contaminated than SPA. The risk factors for a high contamination rate using the TUC technique are patients <6 months of age, difficult catheterization, and uncircumcised boys. In children with urosepsis, it is preferable to consider a permeant catheter in an acute phase. SBC is the easiest method in nontoilet-trained children, but the contamination rate is very high and has high incidence of false-positive results. Therefore, SBC is unreliable in diagnosing UTI.

In conclusion, CMC is an acceptable method for the diagnosis of UTI in toilet-trained children. While SBC is a screening method in nontoilet-trained children and SPA or TUC is mandatory for accurate diagnosis. To ensure the accuracy of the tests, the collected urine specimens must be properly stored to keep fresh (<1 h after voiding at room temperature and <4 h in refrigerator).[11]

Urine analysis

Urinalysis is a fast, noninvasive UTI screening method. However, urinalysis alone is not enough to diagnose a

Table 4: Urine specimen collection method

	Urine bag	Clean catch (CCU/MSU)	Catheterization (CSU)	SPA
Description	After carful cleaning, an adhesive plastic bag is applied to collect urine	The MSU is collected twice after simple retraction of the prepuce in uncircumcised male infants and simple separation of labia majora in female children	After disinfection of the periurethral area, catheter is inserted to catch the urine	After disinfection of suprapubic area and under ultrasound guidance, the urine is aspirated by perpendicular midline puncture with 21-gauge needle, 1 cm above the symphysis pubis
Indications	Unable to collect urine by other methods	Toilet-trained children Parenteral concern regarding CSU and SPA collections	Non toilet-trained infant Acute urinary retention	Nontoilet-trained infant Uncircumcised boys with redundant foreskin or phimosis Girls with labial adhesions Periurethral irritation
Contamination	Highest rate of contamination False positive rate 88%–99%	Greater risk of contamination than catheterization	Potential risk of contamination	Rare
UTI diagnosis	High contamination rate Not suitable to diagnose a UTI	$>10^5$ CFU/mL clinically relevant organisms+pyuria/bacteriuria		Any growth of clinically relevant organisms+pyuria/bacteriuria
Benefits	Noninvasive techniques Negative culture tests may exclude a UTI	Noninvasive technique Preferred technique for children who are able to void on request	Less painful and less invasive than SPA	Preferred aseptic method Less likely to acquire contamination

UTI: Urinary tract infection, MSU: Midstream urine, CCU: Clean catch urine, CSU: Catheter specimens of urine, SPA: Suprapubic aspiration, CFU: Colony-forming unit

UTI. In febrile children, urinalysis can help in identifying who should receive antibacterial treatment while cultures are pending. Dipstick urinalysis indicates the presence of leukocyte esterase (LE) or nitrite, whereas microscopic urinalysis indicates the presence of white blood cell (WBC), WBC cast, and bacteria. Pyuria is the presence of more than 5 WBC per high-power field in a centrifuged sample, whereas bacteriuria is the presence of any bacteria per high-powered field, the presence of one or both requires for UTI diagnosis.

The LE test can be false negative in early UTI and false positive in other febrile diseases, nonspecific vaginitis, or interstitial nephritis. The nitrite test has a relatively high specificity but is not a sensitive marker in children who frequently empty the bladder because Gram-negative bacteria should be present in the bladder for at least 4 h to convert the dietary nitrate to nitrite. Consequently, urinalysis cannot replace a culture of urine but it can be valuable in selecting children with a probable UTI. A positive nitrite with/without LE provides a likely diagnosis of UTI to initiate empirical antibiotic therapy. While a test that is negative for LE and nitrite is highly specific for ruling out UTI. Urine WBC cast is a very significant finding for pyelonephritis, but it quickly resolves (<10 min) in alkaline urine.

To conclude, the interpretation of urinalysis is shown in Table 5: A positive nitrite with/without LE gives a presumptive diagnosis of UTI. A positive LE only may or may not suggest UTI. A negative test for both nitrite and LE suggests no UTI.[11]

Table 5: Diagnosis of urinary tract infection and empirical antibiotic treatment based on urine dipstick test

Urine dipstick	Diagnosis	Antibiotic treatment
Nitrite (+), LE (+)	Possible UTI	Yes
Nitrite (+), LE (−)	Probable UTI	Yes
Nitrite (−), LE (+)	May or may not UTI	Yes or no (depending on clinical conditions)
Nitrite (−), LE (−)	No UTI	No

UTI: Urinary tract infection, LE: Leukocyte esterase

Box 2: Indication for sending urine samples for culture

Suspected upper UTI
Associated comorbidities
Infancy group
Positive result for urine dipsticks
Recurrent UTIs
Child with suspected UTI and nonresponding to treatment within 48 h
When clinical symptoms and dipstick test don't correlate

UTI: Urinary tract infection

Urine culture

In patients with negative urinalysis results, urine culture is unnecessary if there is an alternative cause of fever or inflammatory signs. However, if the results are positive, urine culture confirmation of UTI is mandatory. A urine specimen must be collected correctly in order for a significant amount of Colony Forming Units (CFUs) of a single pathogen to be grown. The indications for culture and sensitivity are shown in Box 2.

The traditional criteria for a positive culture were over 10^5 CFU/ml. Recently, the criterion was reduced to 50,000 CFUs/mL that is obtained through the SPA or TUC. A positive culture of the sterile bag-collected urine may suggest asymptomatic bacteriuria (ASB), which is not a true UTI. Thus, a true UTI must be distinguished from ASB. In symptomatic children with a positive SBC urine culture and abnormal urinalysis, the diagnosis is UTI. While in asymptomatic children with a positive SBC urine culture and normal urinalysis, the diagnosis is ASB.[11]

Blood test

Serum electrolytes and blood cell counts should be obtained for monitoring complicated UTI or if treated with an aminoglycoside for more than 48 h. Screening for G6PD is essential before starting norfloxacin, nitrofurantoin, and trimethoprim/sulfamethoxazole. C-reactive protein has a lower specificity for identifying patients with parenchymal involvement, whereas serum procalcitonin (>0.5 ng/ml) has been used as a reliable serum marker. In a severely ill child with age <3 months, blood and urine cultures should be taken before starting an antibiotic.[10]

DIAGNOSIS

UTI diagnosis is based on clinical symptoms combined with a positive urinalysis that suggests infection (pyuria and/or bacteriuria) and the presence of at least 50,000 CFUs per milliliter of a uropathogen grown from a TUC or SPA urine specimen. Once UTI has been confirmed, the clinician should instruct parents to seek rapid medical evaluation (ideally within 48 h) for future febrile illness to ensure that frequent infections can be detected and treated promptly.[12]

Diagnostic tool

Clinicians should be aware of the indications and limitations of imaging of the urinary tract and use clinical judgment when further imaging is warranted. Table 6 summarizes common urinary tract imaging modalities.

Renal and bladder ultrasound (RBUS) is a basic study that is easy to obtain, safe, and noninvasive test that can reveal the size and shape of the kidneys, the presence of dilatation of the ureters, and the existence of gross anatomic abnormalities. RBUS should be postponed to

Table 6: Renal imaging modalities

KUB ultrasound	MCUG/VCUG	DMSA scan
Uses		
Assess the presence and degree of hydronephrosis or ureteric dilation and signs of urinary tract obstructions or any other renal anomalies Assess the fluid collection and the bladder capacity and postvoid residual	Assess the presence of posterior urethral valves Assess the presence of VUR Assess the bladder capacity, trabeculation and postvoid residual. Gold standard for VUR diagnosis	The gold old standard for renal scar detection and to assess the renal function
Indication		
Concurrent bacteremia Atypical UTI organism: *S. aureus* *Pseudomonas* Infancy age Inadequate response to 48 h of IV antibiotics Abdominal mass Abnormal voiding Recurrent UTI First febrile UTI and no prompt follow done Renal impairment Significant electrolyte disturbance No antenatal renal tract imaging in 2–3 trimester	Abnormal renal ultrasound Hydronephrosis Thick bladder wall Renal scarring Abnormal voiding postfebrile UTI Postsecond febrile UTI Suspicion of VUR and posterior urethral valves	Clinical suspicion of renal injury Reduced renal function Suspicion of VUR And obstructive uropathy
Limitations		
Does not assess function Cannot diagnosis VUR	Radiation exposure Invasive Unpleasant to perform postinfancy	Cannot determine old versus new scarring

MCUG: Micturating cystourethrogram, VCUG: Voiding cystourethrography, VUR: Vesicoureteric reflux, IV: Intravenous, UTI: Urinary tract infection, *S. aureus: Staphylococcus aureus,* DMSA: Dimercapto succinic acid

4–6 weeks after the acute resolution of the infection.[13] It is an advisable and useful method to identify uropathology and renal infections such as pyelonephritis and renal abscess in infants, older children with first febrile UTI, and in patients with recurrent UTIs. It is not reliable in detecting renal scarring or VUR. While the major advantage is the lack of radiation exposure.

RBUS is recommended for the following children:[4]

- Infant or child with UTI, first febrile UTI with no proper follow-up, and recurrent UTI
- Inadequate response to 48 h of intravenous antibiotics, atypical organisms such as *Staphylococcus aureus* and *Pseudomonas*, or coexisting bacteremia
- Abnormal voiding, renal impairment, and significant electrolyte imbalance
- No antenatal renal tract imaging in 2nd to 3rd trimester.

The 2011 AAP Clinical Practice Guidelines support obtaining a renal-bladder ultrasound in all children 2–24 months after the first febrile UTI. Recent literature suggests that the cost-effectiveness of screening with a renal-bladder ultrasound may be increased if sonography is limited to children with a second febrile UTI.

Voiding cystourethrography (VCUG)/micturating cystourethrogram is an invasive study that is still considered the gold standard for excluding or confirming VUR and for assessing the degree of VUR. It should be performed after the first febrile UTI if the ultrasound suggests either high-grade VUR or obstructive uropathy.[12] Furthermore, it is indicated after a second episode of febrile UTI, atypical and recurrent infections in children <2 years of age and in older children, if there is abnormal voiding, which needs to be evaluated for voiding dysfunction with postvoid residual test and referral to urology before they have a VCUG. Likewise, it is indicated if hydronephrosis or thick bladder wall was found on RBUS, non-*E. coli* infection or family history of VUR were noted.[14] The concept of limiting indications for VCUG and dimercaptosuccinic acid (DMSA) scanning is due to significant radiation exposure, catheter risk-induced UTI, stress for young patient and their parents, and considering the cost of imaging techniques.[15]

Where accessible, a nuclear cystogram (NCG) may be used instead of VCUG to evaluate VUR using radioisotopes. It offers a lesser amount of radiation than VCUG but provides poor anatomical detail for the male urethra, so it may miss posterior urethral valves. Using NCG as the initial test for female VUR investigation and in follow-up studies for both genders is reasonable.[15]

Renal scintigraphy (DMSA scan) is a gold standard method for detecting renal parenchymal defects and can be used to detect acute pyelonephritis and renal scarring in acute and chronic settings, respectively. It should be performed

4–6 months later after acute infection and atypical or recurrent infections in children under 2 years of age,[7] and in children with definitive symptoms, negative culture, and normal RBUS. DMSA scans are expensive, invasive, and expose children to radiation.

MANAGEMENT OF URINARY TRACT INFECTION

Treatment aims at eliminating the infection, preventing severe systemic disease, and reducing possible long-term complications such as renal scarring and HTN. The decision to initiate empirical treatment should be based on the disease's clinical suspicion after obtaining history, physical examination, and positive urinalysis on a properly collected specimen of urine.

If the child appears nontoxic and can tolerate oral medication, most patients can be treated as an outpatient. If the diagnosis is uncertain and the child is nontoxic, treatment may be delayed until the results of urine cultures are obtained. In both cases, medicines should be tailored to the results of urine culture-sensitive antibiotics.

The selection of therapy depends on several factors, including the age of the child, underlying medical problems, the severity of the disease, the ability to tolerate oral medications, and most importantly local patterns of resistance to uropathogens.[6] Figures 1-3 present an algorithm for pediatric UTI routine medical management.

Antibiotic treatment should be avoided in ASB without + WBCS in urine analysis unless UTI causes problems or an operative procedure is planned. It is most likely that oral antibiotics will treat uncomplicated UTIs. Each patient should be reassessed 48 h after initiation of antibiotic, and treatment should be modified according to culture and sensitivity.[4] Table 7 summarize the different antibiotic regimen used in children with UTI.

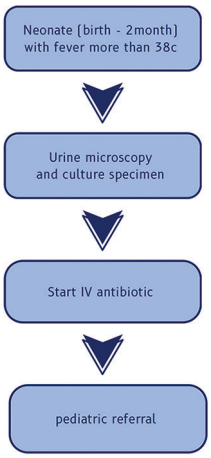

Figure 1: Management approach from birth to 2 months of age

Medical management

Antibiotic treatment should be avoided in ASB without + WBCS in urine analysis unless UTI causes problems or an operative procedure is planned. It is most likely that oral antibiotics will treat uncomplicated UTIs. Each patient should be reassessed 48 h after initiation of antibiotic, and treatment should be modified according to culture and sensitivity.[4] Table 8 summarize the different antibiotic regimen used in children with UTI.

It is recommended that a young infant under 2 months should be referred to a pediatrician and immediately begin parenteral antibiotics. However, the management will vary depending on the severity and location of the infection after this age. Since there is no difference in effectiveness between oral and parenteral therapy, the usual indication for hospitalization and/or parenteral therapy is listed as follows:[16]

- Clinically ill-appearing/toxic appearance
- Severe dehydration/inability to tolerate oral liquids, requiring IV fluids.
- Febrile infant younger than 2 months with severe pyelonephritis.
- Failure to respond to outpatient therapy.
- Suspected obstructive uropathy or high-grade VUR grade (4–5).

When clinical improvement is observed, usually within 24–48 h, parenteral antibiotics should be switched to oral based on the urine culture result. The duration of therapy should be 7–14 days in febrile UTI and pyelonephritis and 3–5 days in afebrile UTI and cystitis, regardless of the route of antibiotic administration.[11]

Choice of antibiotic

The suggestion is to start cephalosporin of the third generation (e.g. cefixime, cephalexin, and cefpodoxime) as the first-line oral agent in the treatment of UTI in children without genitourinary anomalies. If the enterococcal infection is suspected, add amoxicillin or ampicillin. Cephalosporins (e.g. cefotaxime, ceftriaxone, and cefepime) and aminoglycosides (e.g. gentamicin) of the third or fourth generation are suitable first-line parenteral agents for empirical treatment of UTI in children.[17]

Definitive therapy is based on the results and sensitivities of the urine culture. Most patients' clinical condition improves with the initiation of appropriate antimicrobial therapy within 24–48 h. In children, whose clinical condition (other

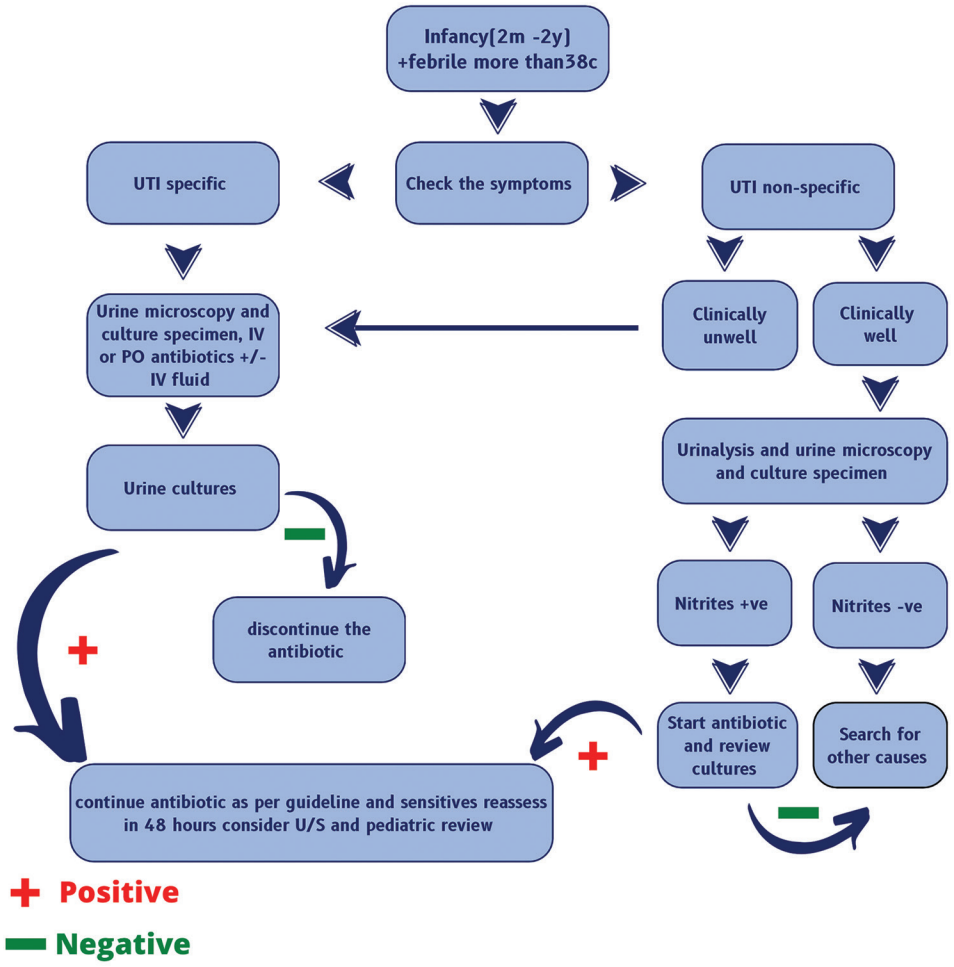

Figure 2: Management approach of children from 2 months to 2 years old

than persistent fever) deteriorates or does not improve as expected within 48 h of antimicrobial therapy initiation and the results of culture and sensitivity are not yet available, the expansion of antimicrobial therapy may be indicated. Most of the above-suggested empirical regimens do not provide adequate *Enterococcus* coverage. In addition, renal and bladder ultrasonography (RBUS) should be performed as soon as possible in children who worsen or fail to improve within 48 h to assess the presence of a renal abscess or surgically correctable anatomic abnormalities or obstruction.[13]

Other therapies

Virus is recognized as the cause of lower UTI, especially hemorrhagic cystitis, among immunocompromised patients, adenovirus, and cytomegalovirus are predominant pathogens, and cidofovir becomes a drug of choice but safety and efficacy are not established in children under the age of 18. It may be difficult to determine the clinical significance of candiduria. Asymptomatic candiduria seldom requires treatment. However, candiduria may be the only microbiological documentation of the candidiasis being disseminated. Candiduria should be treated in symptomatic patients, patients with neutropenia, infants with low birth weight, patients with renal allografts, and patients undergoing urological manipulation. Short therapy courses are not recommended. However, therapy is more likely to be successful for 7–14 days.

Usually, it is helpful to remove urinary tract instruments, including stents and Foley catheters. If complete removal is not possible, it may be beneficial to exchange it. Treatment with fluconazole (200 mg/day for 7–14 days) and amphotericin B deoxycholate has been successful in a wide range of doses (0.3–1.0 mg/kg daily for 1–7 days). In the absence of renal insufficiency, oral flucytosine (25 mg/kg q. i. d.) may be valuable for the eradication of candiduria in urologically infected patients due to *Candida* nonalbicans species.

Subsequently, pediatric infectious disease consultation is recommended if there is no response to treatment within

Table 7: Oral antibiotics regimens for pediatrics urinary tract infection

Antibiotic	Therapeutic dose	Side effect and complication	Bacterial coverage	Contraindication
TMP	Dose not mentioned like the others Not recommended for children younger than 2 months of age	Nausea and vomiting Pruritus Rash, Stevens-Johnson syndrome Hyperkalemia thrombocytopenia leucopenia Have multiple drug interactions	*E. coli* *Enterobacter* spp. *Klebsiella* spp. *P. mirabilis* Coagulase negative S. aureus	In renal impairment and folate deficiency
TMP-SMX	30–60 mg/kg SMZ 6–12 mg/kg TMP Divided Q 12 h Not recommended for children younger than 2 months	Same as TMP Hepatotoxicity Seizures, vertigo Peripheral neuropathy Kernicterus Can lead to pseudomembranous colitis Causes hemolysis in G6PD deficiency	Same as TMP Broader coverage of *Proteus* and *Morganellea* spp.	
Cephalexin	50–100 mg/kg divided Q 8 h	Nausea and vomiting Cholestatic hepatitis Neurotoxicity Blood dyscrasia Headache Risk of Clostridium difficile, Candida and *Enterococcus* spp. Infection	*E. coli* Mirabilia *Klebsiella* spp.	
Augmentin	20–40 mg/kg divided Q 8 h Take with meals to enhance absorption	Rash (are associated with infectious mononucleosis and/or leukaemia Transient disturbance of liver enzymes Nausea and vomiting Diarrhea Cholestatic hepatitis Electrolyte disturbance Neurotoxicity Blood dyscrasia Risk of *Clostridium difficile*, *Candida*, and *Enterococcus* spp. Infection	Useful against b-lactamase strains of *E. coli, Enterobacter* spp. and *Klebsiella* spp.	
Norfloxacin		Rash, pruritis Nausea and vomiting, diarrhea Phototoxicity Hearing loss and diplopia Peripheral neuropathy Tendon rupture Causes hemolysis in G6PD deficiency	*Pseudomonas* spp. Antibiotics resistant bacteria	
Nitrofurantoin	5–7 mg/lg divided Q 6 h Not recommended for children younger than 1 month Antacids reduce potency of drug	Nausea and vomiting, diarrhea Rash Vertigo Peripheral polyneuropathy Urine discoloration Hepatotoxicity is rare Pulmonary toxicity is rare Causes hemolysis in G6PD deficiency	Gram-negative and Gram-positive coverage	
Cefixime	8 mg/kg Q 24 h	Abdominal pain, diarrhea, flatulence, rash		
Cefpodoxime	10 mg/kg divided Q 12 h	Abdominal pain, diarrhea, nausea, rash		
Cefprozil		Abdominal pain, diarrhea, elevated results on liver function tests, nausea		

TMP: Trimethoprim, TMPSMX: TMP-sulfamethoxazole, *P. mirabilis: Proteus mirabilis, S. aureus: Staphylococcus aureus, E. coli: Escherichia coli*

48 h or fever longer than 48–72 h after initiating treatment, if there is an unusual pattern of organism or resistance, and if the patient is severely immunocompromised.[18,19]

Complication

Renal and perinephric abscesses are complications of UTI that usually occur when ascending pyelonephritis is obstructed (usually due to enteric Gram-negative bacilli or polymicrobial infection). Diabetes mellitus and renal stones are the main predisposing conditions for renal and perinephric abscesses. They also occur in the setting of hematogenic seed bacteremia, usually due to *Staphylococcus aureus*. Infections in these sites are sometimes referred to as carbuncles in the renal and perirenal abscesses. Predisposing factors include diabetes mellitus and abnormality of the urinary tract, such as renal stones (especially large stones), VUR, neurogenic bladder, obstructive tumor, benign cyst, or polycystic kidney disease. Clinical manifestations of renal and perinephric abscess are similar to those of acute pyelonephritis: fever, flank pain, abdominal pain, dysuria, and/or frequency. Radiography should be

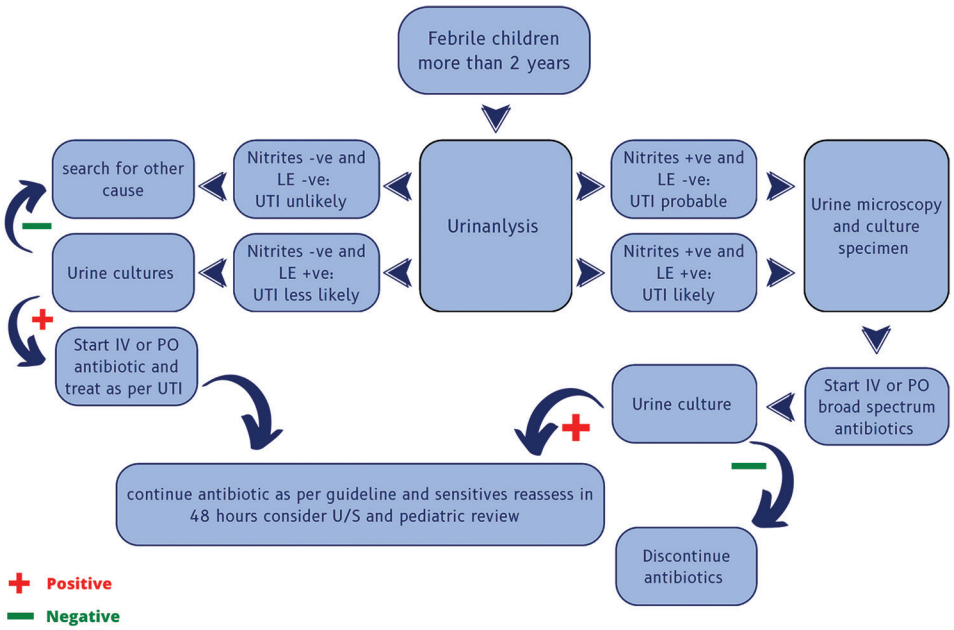

Figure 3: Management approach in children more than 2 years old

Table 8: Antibiotic agent for parenteral treatment of a urinary tract infection

Antibiotic	Threptic dose	Side effect and complication	Bacterial coverage	Contraindication
Ceftriaxone	50–75 mg/kg/day IV/IM as a single dose or divided Q 12 h Do not use it in infant <6 weeks of age	Rash Induration at the site of injection diarrhea Elevated liver enzyme	*E. coli* *P. mirabilis* *M. morganii* *P. vulgaris* *K. Pneumoniae*	
Cefotaxime	150 mg/kg/day IV/IM divided Q 6–8 h Safe to use in infant <6 weeks of age; used with ampicillin in infants aged 2–8 weeks	Rash Induration at the site of injection Diarrhea Elevated liver enzyme Nausea and vomiting		
Ampicillin	100 mg/kg/day IV/IM divided Q 8 h Used with gentamicin in neonate <2 weeks of age And patient allergic to cephalosporins	Rash Diarrhea Pruritus Nausea and vomiting Fever	*Enterococcus* *E. coli* *P. mirabilis*	
Gentamicin	Term neonates <7 days: * 3.5–5 mg/kg/dose IV Q 24 h Infants and children <5 years: * 2.5 mg/kg/dose IV Q 8 h or single daily dosing with normal renal function of 5–7.5 mg/kg/dose IV Q 24 h Children ≥5: * 2–2.5 mg/kg/dose IV Q 8 h or single daily dosing with normal renal function of 5–7.5 mg/kg/dose IV Q 24 h Monitor the kidney function	Neurotoxicity Nephrotoxicity Ototoxicity Rash	*P. aeruginosa* *Proteus species* *E. coli* *Klebsiella*	
Meropenem	Sepsis: 20 mg/kg/dose IV		Multidrug resistance Gram-negative, Gram-positive, and anerobic organisms	
Tazocin	50–100 mg/kg/dose IV or IM		Gram-positive, Gram-negative, anaerobic includes pseudomonas and Group B strep	

M. morganii: Morganella morganii, P. aeruginosa: Pseudomonas aeruginosa, E. coli: Escherichia coli, P. mirabilis: Proteus mirabilis, P. vulgaris: Proteus vulgaris, K. Pneumoniae: Klebsiella pneumoniae, IV: Intravenous, IM: Intramuscular

used for the definitive diagnosis of renal or perinephric abscess; computed tomography and ultrasonography are the most useful modalities.[20-22]

The renal and perinephric abscess management approach includes antimicrobial therapy in conjunction with drainage when warranted. Furthermore, the

urological obstruction should be relieved promptly when present.

Patients with renal abscesses >5 cm should be treated with percutaneous drainage in conjunction with antimicrobial therapy, whereas for renal abscesses <5 cm in diameter, the initial management of antimicrobial therapy (without drainage) is appropriate. If clinical symptoms and radiographic findings persist after several days of therapy, consideration should be given to percutaneous drainage of abscesses <5 cm if technically possible.[20,21] For abscesses not suitable for percutaneous drainage, in severe cases for which medical treatment has failed, surgical drainage and/or rescue nephrectomy may be required. Urological expertise should be consulted when an abscess occurs in the context of an anatomical abnormality, such as large obstructing renal stones or VUR, or when it is too large for effective antibiotic and catheter drainage treatment.[23]

Nephrectomy may also be warranted if the abscess occurs in a small chronically pyelonephritic and poorly functioning kidney that has been destroyed by previous infection episodes.

Drainage catheters should remain in place until the drainage is minimal (usually up to 7 days). Follow-up imaging should be done in the setting of persistent clinical symptoms and laboratory abnormalities, or if the drainage does not proceed as expected. Patients with perinephric abscesses should undergo percutaneous drainage (preferably computed tomography or US-guided) for both diagnostic and therapeutic purposes. If prompt drainage is feasible, it should ideally be done before initiating antimicrobial therapy, so that the results of Gram stain and culture can be used to guide therapy selection.[24-26]

Surgical management

For surgical correctible conditions such as VUR, UPJO, OR UVJO, surgical correction is warranted.

PREVENTION

The natural approach to preventing UTI is more valuable in children. It is no longer preferable to provide antibiotic prophylaxis to children with or without VUR (first to fourth grade). Education is essential for urogenital hygiene and should be properly performed. Physiological phimosis treatment option is topical steroid and circumcision. In labial adhesion, topical steroids and estrogen creams are applied for 2–4 weeks. All dietary factors helped in the prevention of UTI includes breast milk, probiotics, and cranberry should be considered. Adequate intake of fluid is important and addressing the issue of constipation and dysfunctional voiding will be prevented by initiating toilet training at a suitable age (18–24 months) to limit the rate of recurrence of UTI in children.[11]

Follow-up/monitoring

It is not routinely recommended to follow infants with regular urine cultures in ASB. Only follow-up culture should be performed at the onset of unexplained febrile illness. There is also no need to follow any child with normal images. However, recurrent infection and abnormal results of imaging, impaired kidney function, increased blood pressure, and/or proteinuria require close monitoring and evaluation to prevent or slow the progression of chronic kidney disease.[4]

CONCLUSION

Due to the variability of clinical presentations in young and older children with UTI, physicians and clinicians are faced with many challenges to determine the correct approach for diagnosis. Therefore, early diagnosis and management, as well as good preventive strategies and follow-up are important in reducing recurrence and future outcomes. Furthermore, children and their parents need to understand the importance of treatment, compliance, the risk of recurrence, and when to seek a health-care professional for any reinfection. Completing this guidance will require evidence-based information and good decision-making skills to reduce parents' concern and anxiety for the protection of their children.[4]

Author contributions

All authors contributed equally.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Shaikh N, Morone NE, Bost JE, Farrell MH. Prevalence of urinary tract infection in childhood: A meta-analysis. Pediatr Infect Dis J 2008;27:302-8.
2. Beetz R. May we go on with antibacterial prophylaxis for urinary tract infections? Pediatr Nephrol 2006;21:5-13.
3. Spencer JD, Schwaderer A, McHugh K, Hains DS. Pediatric urinary tract infections: An analysis of hospitalizations, charges, and costs in the USA. Pediatr Nephrol 2010;25:2469-75.
4. Desai DJ, Gilbert B, McBride CA. Paediatric urinary tract infections: Diagnosis and treatment. Aust Fam Physician 2016;45:558-63.
5. Hoberman A, Chao HP, Keller DM, Hickey R, Davis HW, Ellis D. Prevalence of urinary tract infection in febrile infants. J Pediatr 1993;123:17-23.
6. Shaw KN, Gorelick M, McGowan KL, Yakscoe NM, Schwartz JS.

Prevalence of urinary tract infection in febrile young children in the emergency department. Pediatrics 1998;102:e16.
7. Schmidt B, Copp HL. Work-up of pediatric urinary tract infection. Urol Clin North Am 2015;42:519-26.
8. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. Int J Surg 2010;8:336-41.
9. Wein AJ, Partin AW, Peters CA. Campbell-Walsh Urology. 11th ed. Elsevier: Philadelphia, PA; 2012.
10. Stein R, Dogan HS, Hoebeke P, Kočvara R, Nijman RJ, Radmayr C, *et al*. Urinary tract infections in children: EAU/ESPU guidelines. Eur Urol 2015;67:546-58.
11. Lee SJ. Clinical guideline for childhood urinary tract infection (Second Revision). Child Kidney Dis 2015;19:56-64.
12. Hooten JT, Sch frag RJ, Barshes JP, Liu KD, Baum LK, Wo¨rner AJ, *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 2018;141:e20181706. doi: 10.1542/peds.2018-1706.
13. Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management, 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;128:595-610.
14. Ismail SI. Urinary tract infection in children: NICE guideline. Trends Urol Gynecol Sex Health 2008;13:12-3.
15. Alejandro Hoberman M, Klein JO, Okafor KK, Pelton SI. Acute management, imaging, and prognosis of urinary tract infections in infants and children older than one month. UpToDate: Waltham, MA; 2018.
16. Consensus Guidelines for Management of Pediatric Urinary Tract Infection (UTI): Northern California Pediatric Hospital Medicine Consortium; 2018.
17. Hoberman A, Wald ER, Hickey RW, Baskin M, Charron M, Majd M, *et al*. Oral versus initial intravenous therapy for urinary tract infections in young febrile children. Pediatrics 1999;104:79-86.
18. Pappas PG, Kauffman CA, Andes D, Benjamin DK Jr., Calandra TF, Edwards JE Jr., *et al*. Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009;48:503-35.
19. Fisher JF, Sobel JD, Kauffman CA, Newman CA. Candida urinary tract infections-treatment. Clin Infect Dis 2011;52 Suppl 6:S457-66.
20. Dembry LM, Andriole VT. Renal and perirenal abscesses. Infect Dis Clin North Am 1997;11:663-80.
21. Fowler JE Jr., Perkins T. Presentation, diagnosis and treatment of renal abscesses: 1972-1988. J Urol 1994;151:847-51.
22. Coelho RF, Schneider-Monteiro ED, Mesquita JL, Mazzucchi E, Marmo Lucon A, Srougi M. Renal and perinephric abscesses: Analysis of 65 consecutive cases. World J Surg 2007;31:431-6.
23. Siegel JF, Smith A, Moldwin R. Minimally invasive treatment of renal abscess. J Urol 1996;155:52-5.
24. Gerzof SG, Gale ME. Computed tomography and ultrasonography for diagnosis and treatment of renal and retroperitoneal abscesses. Urol Clin North Am 1982;9:185-93.
25. Kuligowska E, Newman B, White SJ, Caldarone A. Interventional ultrasound in detection and treatment of renal inflammatory disease. Radiology 1983;147:521-6.
26. Lang EK. Renal, perirenal, and pararenal abscesses: Percutaneous drainage. Radiology 1990;174:109-13.