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URINARY TRACT INFECTION: A SYSTEMATIC REVIEW OF EPIDEMIOLOGY, DIAGNOSIS AND TREATMENT IN PEDIATRICS

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ABSTRACT

Objective: The general objective of the present study is to analyze the scientific production on urinary tract infection in pediatrics, seeking to identify the main methods used in the diagnosis and treatment of this pathology. Methodology: This is a systematic review focused on understanding the main aspects that permeate urinary tract infection in the pediatric population. The research was guided by the question: "What are the main aspects that permeate urinary tract infection in pediatrics, as well as what are the diagnostic and therapeutic resources used in clinical practice?". To find answers, searches were performed in the PubMed database using four descriptors combined with the Boolean term "AND". This resulted in 242 articles. 20 articles were selected for analysis and 13 articles were used to compose the collection. Results: Urinary tract infections (UTIs) in children require careful diagnosis and treatment due to their variability in incidence and diversity of pathogens. Proper choice of antibiotics and continuous antibiotic prophylaxis (CAP) are essential for effective management and prevention of recurrences, especially in cases of anatomical abnormalities of the urinary tract. Conclusion: Preventive measures, such as hygiene and judicious use of antibiotics, are essential to reduce the occurrence of UTIs and

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improve children's quality of life. An integrated approach, combining therapeutic and preventive strategies, is crucial to minimize long-term complications and promote pediatric health.

Keywords: Pediatrics. Urinary tract infection. Treatment. Diagnosis.

INTRODUCTION

Urinary tract infections (UTIs) are among the most common bacterial infections in children. Up to 8% of children will have at least one UTI between 1 month and 11 years, and up to 30% of infants and children have recurrent infections during the first six to 12 months after the initial UTI. In the United States, there are about 1.5 million pediatric outpatient visits annually for UTIs.5 Overall U.S. healthcare costs for UTI management and treatment in 2013 were $630 million. UTIs cause short-term morbidity, such as fever, dysuria, and flank pain, and can also result in long-term kidney injury, such as permanent kidney scarring (OLIVEIRA et al., 2020).

UTIs can lead to long-term consequences such as kidney scarring, hypertension, and even end-stage kidney disease. The incidence of UTI in pediatrics varies depending on age, race, ethnicity, sex, and circumcision status. The range of incidences reaches significantly high in each gender throughout the first year of life during a symptomatic UTI for the first time. Boys have a higher incidence than girls in the first year of life, after which the rate drops, and girls (7.5%) predominantly suffer from UTI, which is 2 to 4 times higher than boys (2.4%). The prevalence of UTI in uncircumcised boys (20.1%) is 10 times higher than in circumcised boys (2.4%) (ALSAYWID et al., 2023).

Bacterial aggression of the urinary tract produces symptoms (dysuria, urgency and frequency of urination, hematuria, low back pain, and fever) in older children, whereas the signs and symptoms of UTIs in infants are nonspecific: lethargy, irritability, anorexia, fever, and neonates may develop bacteremia. UTIs should be suspected in all infants with fever of unknown origin; on the other hand, fever may be absent in a very sick newborn (MARINGHINI; ALAYGUT; CORRADO, 2024). A recurrent UTI is defined as an individual who is diagnosed with 2 or more UTIs in a 6-month period, or 3 in a 1-year period. The two risk factors that have been shown to have the highest 2-year recurrence rate for UTI are vesicoureteral reflux (VUR) and bladder and bowel dysfunction (BBD), with the combination of both producing an even higher risk (56%). Risk factors for kidney scarring after febrile UTI include children with high-grade reflux, late initiation of antibiotics after 72 hours, recurrent UTIs, infectious organisms other than E. coli, and older age. Laboratory findings associated with renal scarring are fever (>39 °C), polymorphonuclear count>60%, CRP>40 mg/L, and an abnormal finding on renal and bladder ultrasound (RBUS) (OLSON; DUDLEY; ROWE, 2022).

UTIs are estimated to account for 5–14% of annual pediatric emergency department visits, necessitating the prescription of large volumes of antibiotics in healthcare. However, large-scale antibiotic prescribing is strongly associated with the occurrence of antimicrobial resistance (AMR) in bacteria, often leading to increased resistance to first-line antibiotics for UTIs, such as trimethoprim and penicillins. Over-prescription is also responsible for the emergence of resistance to cephalosporins, such as extended-spectrum B-lactamase (ESBL)-producing bacteria (VAZOURAS et al., 2023).

This systematic review article aims to compile and evaluate the existing scientific evidence on urinary tract infection in the pediatric population. The intention is to provide a comprehensive and up-to-date view, which not only synthesizes current knowledge about the condition, but also identifies gaps in research and directs future investigations and clinical practices. By offering an in-depth analysis of the evidence, this study aims to serve as a resource for health professionals, researchers, and academics, helping to optimize diagnostic and therapeutic approaches to this condition.

METHODOLOGY

This is a systematic review that seeks to understand the main aspects of urinary tract infection in the pediatric population, as well as to demonstrate the main diagnostic and pharmacological methods used in the treatment of the condition. For the development of this research, a guiding question was elaborated through the PVO (population, variable and objective) strategy: "What are the main aspects that permeate urinary tract infection in pediatrics, as well as what are the diagnostic and therapeutic resources used in clinical practice?"

The searches were carried out through searches in the PubMed Central (PMC) databases. 4 descriptors were used in combination with the Boolean term "AND": Urinary tract infections, Pediatrics, Diagnosis of urinary tract infections and Treatment of urinary tract infections. The search strategy used in the PMC database was: Urinary tract infections AND Pediatrics and Diagnosis of urinary tract infections AND Pediatrics AND Treatment of urinary tract infections. From this search, 242 articles were found, which were later submitted to the selection criteria. The inclusion criteria were: articles in English, Portuguese and Spanish; published in the period from 2019 to 2024 and that addressed the themes proposed for this research, in addition, review, observational and experimental studies, made available in full. The exclusion criteria were: duplicate articles, available in the form of abstracts, that did not directly address the proposal studied and that did not meet the other inclusion criteria.

After associating the descriptors used in the searched databases, a total of 242 articles were found. After applying the inclusion and exclusion criteria, 20 articles were selected from the PubMed database, and a total of 13 studies were used to compose the collection.

RESULTS

Authors Cited	Main Contributions to the Systematic Review
Oliveira et al., 2020	UTIs are common in children, with costs of $630 million in the U.S. in 2013. E. coli is the predominant bacterium responsible for UTIs, especially acute pyelonephritis. Other organisms include Proteus mirabilis, Klebsiella spp., and Staphylococcus saprophyticus. Capsular polysaccharides confer resistance to the host's defenses. Hemolysins are cytotoxic proteins that cause acute pyelonephritis. Uropathogenic bacteria compete with host cells for nutrients such as iron. LPS activates Toll-like Receptor 4 (TLR4) signaling.
Alsaywid et al., 2023	UTIs can cause kidney scarring, hypertension, and end-stage kidney disease. Incidence varies by age, race, ethnicity, sex, and circumcision status. Boys have a higher incidence in the first year, girls (7.5%) suffer more from UTI later. Uncircumcised boys (20.1%) have a higher prevalence than circumcised boys (2.4%). UTI classifications include location, severity, episode, symptoms, and complicating factors. Uncomplicated UTI occurs in patients with normal urinary tract and competent immune system. Complicated UTI occurs in children with known mechanical or functional pathology of the urinary tract. Community-acquired UTIs usually caused by Enterobacteriaceae or Enterococcus faecalis. Nosocomial UTIs caused by Escherichia coli or Pseudomonas. Diagnosis of UTI is based on clinical symptoms combined with positive urine analysis. Urine collection should be performed prior to the use of antibiotics. Proper urine collection is crucial for diagnosis.
Maringhini; Alaygut; Corrado, 2024	Signs and symptoms of UTIs in older children include dysuria, urgency, frequency of urination, hematuria, low back pain, and fever. In infants, symptoms are nonspecific. Definition of recurrent UTI and risk factors for renal scarring. The number of colonies obtained by urine culture is critical for the diagnosis of UTI. Leukocyte esterase (LE) and nitrite tests are helpful, but final evaluation should be with urine culture. NGAL has higher sensitivity but higher cost.
Olson; Dudley; Rowe, 2022	UTIs can cause kidney scarring, with risk factors such as vesicoureteral reflux, late initiation of antibiotics, and older age. Laboratory findings associated with renal scarring include high fever, high polymorphonuclear count, and elevated CRP. Diagnosis of UTI based on clinical symptoms and positive urine analysis. The American Academy of Pediatrics defines UTI as the presence of at least 50,000 CFU/mL of a single uropathogen obtained by urinary catheterization with a positive leukocyte esterase (LE) dipstick urine analysis. Urine collection should be performed prior to the use of antibiotics. The purpose of the image is to identify genitourinary anomalies. CEVUS is a radiation-free method for evaluating VUR. DMSA identifies kidney scars but has radiation exposure.
Vazouras et al., 2023	UTIs account for 5-14% of pediatric emergency department visits. Over-prescribing antibiotics is associated with antimicrobial resistance, leading to resistance to first-line antibiotics and cephalosporins.
A'T Hoen et al., 2021	UTIs are bacterial infections that are most common in children. Symptoms vary with age. In neonates, males predominate and have a higher risk of urosepsis. Pooled prevalence of 7.8% in children <19 years with urinary symptoms. Incidence in boys is higher in the first 6 months (5.3%) and decreases with age. In girls, UTIs increase with age (2% to 11%). UTI is nonspecific in infants and young children. Classification of UTIs based on the complication of the condition: Uncomplicated UTI occurs in patients with normal urinary tract and competent immune system; Complicated UTI occurs in children with known mechanical or functional pathology of the urinary tract. Treatment of UTIs depends on age, disease severity, and local antimicrobial resistance. Parenteral antibiotic therapy recommended for neonates and infants younger than 2 months.
Agrawal; Paunikar, 2024	Candida species can cause fungal UTIs in certain clinical scenarios. Viral cystitis can be caused by adenovirus and herpes simplex, although it is less common than bacterial infections. Hematogenous spread, especially from fungal and staphylococcal infections, is more common in ill, blocked, or immunocompromised individuals.
Autore et al., 2023	Risk factors for recurrent UTIs in pediatrics include congenital urinary tract abnormalities, chronic constipation, bladder dysfunction, neurogenic bladder, gender, and poor hygiene.

	Permanent renal scarring may occur in 15% of the first episodes of UTI and in 40% of all cases, and may lead to proteinuria, hypertension, and renal failure.
Nelson et al., 2024	CT scans are not useful in the routine initial diagnosis of cystitis or pyelonephritis. CT imaging may be useful if symptoms persist or worsen beyond 72 hours, or if there are concerns about kidney stones, renal abscesses, or an alternate focus of infection. Ultrasound is a preferable first-imaging modality in younger patients, pregnancies, and/or kidney transplant recipients. Contrast-enhanced or non-contrast-enhanced MRI is less effective for early detection of disease and visualization of stones, but may have an advantage in identifying graft infection.
Buettcher et al., 2021	Treatment of UTIs in children depends on age, disease severity, presence of gastrointestinal symptoms, and medical and/or urological comorbidities. Parenteral antibiotic therapy recommended for neonates and infants younger than 2 months. Treatment for 7 to 10 days is considered safe in young children < 90 days. Oral administration of antibiotics is effective unless the patient is not taking the drug. Duration of treatment should be 3 to 5 days in case of cystitis and 10 to 14 days in case of pyelonephritis.
Ammenti et al., 2020	The choice of antibiotic should be based on local conditions of antimicrobial susceptibility and adjust according to the susceptibility test of the uropathogen alone. Escherichia coli remains the predominant uropathogen in acute uncomplicated community-acquired infections (80%), followed by Klebsiella, Enterobacter, Proteus species, and Enterococci.
Alsaywid et al.	Adenovirus and cytomegalovirus are predominant pathogens. Cidofovir is a treatment option; Safety and efficacy are not established in children under 18 years of age. Asymptomatic candiduria rarely requires treatment; symptomatic candiduria should be treated with fluconazole or amphotericin B. Removal of urinary tract instruments is recommended.
Alsubaie; Barry	Antibiotic prophylaxis to prevent recurrent UTIs in children with and without anatomical complications. Use of antibiotics such as nitrofurantoin and TMP-SMX for 6 to 12 months. Switching antibiotics if there is a resistant microorganism. Intravesicular irrigation with aminoglycoside can be used in children with neurogenic bladder.

DISCUSSION

Urinary tract infections (UTIs) represent the most common bacterial infections in children. Symptoms can vary according to the age of the child. In neonates, there is a predominance of males, the prevalence is higher, infections caused by organisms other than E. Coli are more frequent, and there is a greater risk of urosepsis. A pooled prevalence of 7.8% of UTI was observed in older children (<19 years) presenting with urinary tract symptoms. The incidence varies with age and sex. The incidence in boys is highest during the first 6 months of life (5.3%) and decreases with age to about 2% at ages 1 to 6 years. In girls, the incidence is reversed, with UTIs being less common during the first 6 months (2%) and increasing with age to about 11% at ages 1 to 6 years (A'T HOEN et al., 2021).

The urinary tract is normally sterile, except for the distal part of the urethra. Physiologically, the periurethral area has gut bacteria. In healthy young girls, the predominant bacterium is Eschericha coli (E. coli), while in boys, after the first 6 months of life, Proteus mirabilis predominates. On the other hand, gut bacteria usually do not form the periurethral flora of older children. It should be noted, however, that colonization with Gram-negative bacteria usually precedes the occurrence of UTI. On some occasions, the prescription of broad-spectrum antibiotics for other infections can produce changes in the normal flora. E. coli is responsible for 80-90% of episodes of acute community-acquired pyelonephritis, especially in children. Less common uropathogenic bacteria include Proteus mirabilis, Klebsiella spp., and Staphylococcus saprophyticus. UTI infectious agents acquired during hospitalization depend on the hospital environment and underlying host factors (OLIVEIRA et al., 2020).

In certain clinical scenarios, Candida species can lead to fungal UTIs, while viral cystitis can be caused by viruses such as adenovirus and herpes simplex, although less commonly than bacterial infections. Parasitic UTIs are rare in developed countries, but they can occur in regions where specific parasites are endemic. Hematogenous spread, particularly of fungal and staphylococcal infections, is more common in sick, blocked, or immunocompromised individuals (AGRAWAL; PAUNIKAR, 2024).

UTI can occur by two routes: hematogenous and ascending. The hematogenous pathway is typical in newborns, while the ascending pathway characteristically develops after the neonatal period. In neonates, UTI can present as sepsis, largely with nonspecific clinical features, including anorexia, vomiting, poor sucking, irritability, lethargy, seizures, pallor, hypothermia, and sometimes jaundice. As with most infections, in this age group, there is a high probability of bacteremia and a high mortality rate (around 10%) due to the spread of the infection to other sites, leading to meningitis, for example. The ascending pathway comprises the migration, fixation, and proliferation of uropathogenic bacteria in the urinary tract. Uropathogenic bacteria can reside for long periods in the gastrointestinal tract before spreading to the periurethral area. After spreading through the perineum to the periurethral area, the bacteria ascend through the urinary tract against the flow of urine and establish the infection through various mechanisms. The main mechanisms include fimbriae that promote adhesion to urothelial cells, flagella-mediated motility, resistance to antibacterial defenses, and other adaptation strategies. In this sense, the subtype of E. coli strain that causes acute pyelonephritis in healthy children has genes that confer virulence, forming the so-called "islands of pathogenicity" (OLIVEIRA et al., 2020).

Sequential activation of these genes increases attack on host tissue and bacterial survival. The presence of fimbriae promotes bacterial adhesion to the mucosa that facilitates attack on the tissue, increasing exposure to other virulence factors, such as hemolysin and lipopolysaccharide (LPS). These toxins secreted by E. coli can affect cellular functions or induce cell death. Uropathogenic strains of E. coli can be identified by the presence of surface antigen expression (OKH serotypes) or surface expression of P. fimbria. Type 1 fimbriae bind to mansilate epitopes present in the Tamm-Horsfall glycoprotein, secretory immunoglobulin A (IgA), bladder cell uroplatines, or integrin molecules.35---37 S fimbriae bind to receptors on sialylated glycoproteins and glycolipids, while P fimbriae recognize Gal1-4Gal epitopes on glycolipids, which are antigens in the P blood group system. capsular polysaccharide and hemolysin. LPS is an endotoxin of Gram-negative bacteria that contains lipid A anchored to the outer membrane, as the component responsible for toxic effects, including fever and acute phase response. Other components of LPS are the oligosaccharide nucleus and the repeated oligosaccharide that determines the O antigen. LPS activates Toll-like receptor 4 (TLR4) signaling, after binding to soluble CD14 or associated with the cell surface (OLIVEIRA et al., 2020).

Capsular polysaccharides are formed from oligosaccharide polymers that surround bacteria. The capsules give bacteria resistance against the host's defenses, neutralizing the lytic effects of complement and phagocytosis. Hemolysins are cytotoxic, pore-forming proteins that permeate the cell membrane. Hemolysin production was first observed in the 1940s in E. coli, causing acute pyelonephritis. In addition to virulence mechanisms, uropathogenic bacteria can also compete with host cells for nutrients, such as iron. All uropathogenic strains express some molecules responsible for iron uptake. For example, enterobactin is expressed by almost all E. coli strains, but most E. coli strains causing acute pyelonephritis produce aerobactin, which is a high-affinity iron-binding protein, as well as other iron-sequestering proteins, including yersiniabactin, ChuA (OLIVEIRA et al., 2020).

Risk factors for recurrent UTIs in pediatric age include congenital abnormalities in the urinary tract (i.e., vesicoureteral reflux (VUR), ureteropelvic junction obstruction, urethral valves), chronic constipation, voiding bladder dysfunction or incomplete bladder emptying, neurogenic bladder, gender, and poor bathroom hygiene Although acute septic complications are uncommon, permanent renal scarring may occur in 15% of first episodes of UTI and in 40% of the total cases. Loss of kidney function can lead to proteinuria, hypertension, and kidney failure (AUTORE et al., 2023).

Urinary tract infections are classified according to five systems: location, severity, episode, symptoms, and complicating factors, of which location and severity are the most important. Lower urinary tract infection (cystitis) is an inflammatory condition of the bladder mucosa. Symptoms include dysuria, increased urinary frequency, urgency, enuresis, hematuria, suprapubic pain, and foul-smelling urine. It can also include epididymitis, which is an inflammatory condition of the epididymis. Symptoms include pain and swelling of the hemisphere and may be the presenting symptom of lower urinary tract infection. Upper urinary tract infection, called pyelonephritis, is a diffuse pyogenic infection of the renal pelvis and parenchyma. Symptoms include fever, chills, and flank pain, and can be as severe as septic shock/toxemia. A UTI is classified as mild when children have mild symptoms and are able to take fluids and oral medications, usually due to a lower urinary tract infection. If they have more serious symptoms, such as persistent vomiting, dehydration, or fever >39 C, which is classified as a severe UTI (A'T HOEN et al., 2021).

UTI is nonspecific in infants and young children and is more evident as the child grows. 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 location, episode, symptoms, and complicating factors are recognized by obtaining the patient's history, which includes questions about primary or recurrent infection, febrile or non-febrile UTIs, and urinary tract malformation (pre- and/or postnatal ultrasound findings). In addition to a family history of urologic abnormalities, particularly VUR, previous surgery, drinking and urinating. Other relevant histories include bowel habits (history of constipation), amount of fluid intake, presence of lower urinary tract symptoms, and sexual history in adolescents. 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 the fever. Physical examination should assess whether the patient is sick or well, assess hydration status, along with examination of the abdomen to exclude any palpable kidney or bladder, external genitalia to exclude any genital disorder, and lower limbs. Conditions such as spina bifida, phimosis, lip adhesions, or signs of sexual abuse may be presented (ALSAYWID et al., 2023).

Another classification used is based on the complication of the condition. In uncomplicated UTI, infection occurs in a patient with morphologically and functionally normal upper and lower urinary tract, normal renal function, and competent immune system. Patients may be treated on an outpatient basis, followed by elective evaluation for potential anatomical or functional abnormalities of the urinary tract. A complicated UTI occurs in children with known mechanical or functional pathology of the urinary tract. Patients with complicated UTI require hospitalization and parenteral antibiotics. Prompt anatomical evaluation of the urinary tract is critical to exclude the presence of significant abnormalities, and when present, adequate drainage of the infected urinary tract is required (A'T HOEN et al., 2021).

UTIs can also be defined by their relationship to other UTIs; a first infection 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 a previous 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 the outside into the urinary tract. Persistence refers to a recurrent UTI caused by the same bacteria targeting the urinary tract, 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 gut (e.g., Enterobacteriaceae or Enterococcus faecalis) that are susceptible to most antimicrobials. Nosocomial or health-related UTIs occur in hospitalized or institutionalized patients, usually caused by Escherichia coli or Pseudomonas and other more antimicrobial-resistant strains (ALSAYWID et al., 2023).

The diagnosis of UTI is based on clinical symptoms combined with a positive urine test that suggests infection (pyuria and/or bacteriuria). The American Academy of Pediatrics defines a UTI as the presence of at least 50,000 CFU/mL of a single uropathogen obtained by urinary catheterization with a positive dipstick urine analysis for leukocyte esterase (LE) or leukocytes present on urine microscopy. Due to the high sensitivity of LE, it is commonly used to rule out UTI in its absence. Nitrites have a higher specificity and are therefore used to rule out disease. The presence of bacteria, leukocytes, and red blood cells on urine microscopy can add confirmation to the diagnosis. Once UTI has been confirmed, the clinician should instruct parents to seek a prompt medical evaluation (ideally within 48 h) for future febrile illnesses to ensure that frequent infections can be detected and treated promptly (ALSAYWID et al., 2023) (OLSON; DUDLEY; ROWE, 2022).

Urine collection should be obtained if unexplained fever is greater than 38°C and features of UTI are suspected before using any antibacterial agent. Urine collection in infants will be challenging, non-invasive techniques include a sterile pouch applied to the perineum, sterile pouch collection (SBC), and clean urine collection from the middle of the jet, while invasive methods include transurethral catheterization (TUC) and suprapubic aspiration (SPA). Appropriate urine collection should complete the diagnosis of UTI. 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 advantages and disadvantages, the best way to select is according to age, symptom severity, and toilet training status. Clean mid-stream urine collection (CMC) is the method of choice for diagnosing UTI in children trained to use the toilet, mid-stream urine is collected twice. SPA is a gold standard method in children who are not toilet trained with an 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. Risk factors for a high rate of contamination 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. BCS is the easiest method in untoilet trained children, but the contamination rate is very high and has a high incidence of false-positive results. Therefore, BCS is not reliable in diagnosing UTI (ALSAYWID et al., 2023) (OLSON; DUDLEY; ROWE, 2022).

The number of colonies is critical for the diagnosis of UTI and can be obtained by a urine culture. A UTI is defined as the growth of a single pathogen with a colony count of 50,000 CFU/mL or a colony count between 10,000 and 50,000 CFU/mL, with associated pyuria detected on urine analysis done on urine samples obtained by bladder catheterization in older children, whereas the optimal definition for a UTI in neonates has not been established. In the case of SPA, any 1000 CFU/mL growth colony count of a urinary pathogen is significant. Urine dipsticks are easy to obtain, and dipstick analysis includes testing for leukocyte esterase (a marker for pyuria) and nitrite (a marker for Enterobacteriaceae), which is helpful, but the final evaluation should be performed with a urine culture. The urinary neutrophil gelatinase-associated lipocalin (NGAL) test has a higher sensitivity but is more expensive; additional studies are needed to determine the usefulness of urinary NGAL as a screening test for UTI (MARINGHINI; ALAYGUT; CORRADO, 2024).

The purpose of imaging is to identify genitourinary anomalies that increase the risk of recurrent UTI and injuries from repeated infections (renal scarring, renal failure). A renal and bladder ultrasound (RBUS) should be obtained in all infants aged 2 to 24 months after the first febrile UTI. Children older than 2 to 24 months who have recurrent febrile UTI should also be evaluated, although UBI has low sensitivity for detecting mild to moderate VUR or for recurrent febrile UTI. MCU is used to identify children with high-grade reflux (IV–V) who are at risk for kidney deterioration, but should be used selectively given the need for catheterization and radiation exposure Contrasted voiding urosonography (CEVUS) has emerged as a radiation-free method to evaluate children with VUR. The method works by using echogenic microbubbles containing contrast that are easily detected using low mechanical index ultrasound. The diagnostic accuracy of CEVUS for VUR is excellent, with recent studies citing a sensitivity of 90.4–92% and a specificity of 92.8–98%. The agreement with VCUG for detection and classification of VUR is 84.3% and 81.8%, respectively, with a multitude of data confirming the non-inferiority of CEVUS when compared to VCUG (OLSON; DUDLEY; ROWE, 2022).

Dimercaptosuccinate (DMSA) scans can be used to identify patients with kidney scars, however, they are also sensitive to detect kidney anomalies such as small or missing kidneys, ectopic kidneys, and duplex systems. The AUA recommends DMSA scans when the initial UBI is abnormal or when there is a concern about kidney scarring (rupture UTIs). A DMSA scan has a higher sensitivity for detecting renal parenchymal lesions when compared to RBUS; however, inflammatory changes in the kidney can cause false-positive scans if performed within the first 4–6 months after an infection, increases the risk of kidney damage, and is often self-limiting; therefore, the use of VCUG has become increasingly selective. Data show that less than 40% of children have VUR after their first febrile UTI, and among this group, less than 10% have high-grade VUR (IV,V). Similar to VCUG, the pitfall of DMSA is radiation exposure, with one study proving that the average exposure per scan is 2.84 mSv, the equivalent of 28 chest X-rays per year. DMSA can also be difficult for radiologists to obtain (OLSON; DUDLEY; ROWE, 2022).

Computed tomography (CT) scans do not appear to be useful in the routine initial diagnosis of cystitis or pyelonephritis and may not routinely alter treatment. CT imaging may be useful if symptoms persist or worsen beyond 72 hours, or if there are concerns about kidney stones, renal abscesses, or an alternative focus of infection. Contrast-enhanced CT images are best discussed with the radiologist, but may have advantages in terms of detecting renal abscesses. Ultrasonography, while safer and more affordable, has limited accuracy, but may be a preferable first-imaging modality in younger patients, pregnancies, and/or kidney transplant recipients because there is no ionizing radiation and can more directly visualize the transplanted organ(s). Contrast- or non-contrast-enhanced and/or diffusion-weighted imaging MRI is less effective for early detection of disease and visualization of stones, but it may also have an advantage in identifying graft infection (NELSON et al., 2024).

In general, treatment for children with suspected UTI depends on the child's age, the severity of the disease, the presence of concomitant gastrointestinal symptoms (e.g., vomiting), underlying medical and/or urologic comorbidities, and local patterns of antimicrobial resistance. Because there is an increased incidence of urosepsis in neonates and infants less than 2 months of age, it is recommended to initiate parenteral antibiotic therapy. There is currently little evidence available to guide the total duration of antimicrobial therapy in children with febrile UTIs. However, treatment for periods of 7 to 10 days is also considered safe in young children < 90 days (BUETTCHER et al., 2021).

The discomfort of a UTI can be relieved by antibiotic treatment. A large number of antibiotics are effective in treating UTIs. The type of medication is usually guided by a urine culture, but most antibiotics are effective. Oral administration has been proven to be effective unless the patient is not taking the drug. The duration of treatment should be 3 to 5 days in case of cystitis and 10 to

14 days in case of pyelonephritis, limiting intravenous antibiotics to a few days followed by oral therapy. The suggestion is to initiate third-generation cephalosporin (e.g., cefixime, cephalexin, and cefpodoxime) as a first-line oral agent in the treatment of UTI in children without genitourinary anomalies. If enterococcal infection is suspected, add amoxicillin or ampicillin. Third- or fourth-generation cephalosporins (e.g., cefotaxime, ceftriaxone, and cefepime) and aminoglycosides (e.g., gentamicin) are first-line parenteral agents suitable for the empirical treatment of UTI in children. Definitive therapy is based on the results and sensitivities of urine culture. The clinical condition of most patients improves with initiation of appropriate antimicrobial therapy within 24–48 h (ALSAYWID et al., 2023) (MARINGHINI; ALAYGUT; CORRADO, 2024).

The choice of antibiotic should be based on the standard local conditions of antimicrobial susceptibility (if available) and adjust according to the susceptibility test of the uropathogen alone. Escherichia coli remains the predominant uropathogen isolated in acute uncomplicated community-acquired infections (80%), followed by Klebsiella, Enterobacter, Proteus species, and Enterococci. Many of them the characteristics of these pathogens are changing, mainly due to antimicrobial resistance (AMMENTI et al., 2020).

Risk factors for renal scarring are multiple episodes of acute pyelonephritis (APN), high-grade VUR, bacterial virulence, and delay in antibiotic treatment, especially in infants with signs of nonspecific UTI. Proper antibiotic treatment is the most effective treatment option for UTI, but it may not be enough to prevent kidney scarring. Corticosteroids may play a role in reducing kidney scarring and urine cytokine levels. Cytokines can predict the severity of kidney damage, playing a key role in kidney scarring after APN, as they represent the mediators of an inflammatory process in response to an infection Some studies have attempted to examine the hypothesis that corticosteroids may affect cytokine response and decrease kidney damage after APN (GKIOURTZIS et al., 2023).

The 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 18 years of age. It may be difficult to determine the clinical significance of candiduria. Asymptomatic candiduria rarely requires treatment. However, candiduria may be the only microbiological documentation of candidiasis being disseminated. Candiduria should be treated in symptomatic patients, patients with neutropenia, low birth weight infants, patients with renal allografts, and patients undergoing urologic manipulation. Short courses of therapy are not recommended. However, therapy is more likely to be successful for 7 to 14 days. It is usually useful to remove instruments from the urinary tract, including stents and Foley catheters. If complete removal is not possible, it may be beneficial to change it. Treatment with fluconazole (200 mg/day for 7–14 days) and amphotericin B deoxycholate has been successful over a wide range of doses (0.3–1.0 mg/kg daily for 1–7 days). In the absence of renal failure, oral flucytosine (25 mg/kg qid) may be valuable for the eradication of candiduria in patients urologically infected due to the species Candida nonalbicans (ALSAYWID et al., 2023).

Continuous antibiotic prophylaxis (CAP) was initially introduced for prevention of recurrent UTIs without any results from controlled clinical studies. Based on the results of clinical studies, CAP was later proposed to prevent recurrent UTIs in children with anatomical abnormality in the urinary system, prenatal hydronephrosis, and/or VUR. The practice was recommended by some treatment guidelines, although it was based on limited data. Over time, the practice of CAP has been expanded to prevent UTIs in children without complications such as VUR, hydronephrosis, or anatomical abnormalities. When indicated, CAP can be given for 6 to 12 months using narrow-spectrum antibiotics such as nitrofurantoin (at a dose of 1 mg/kg/d) or TMP-SMX (at a dose of 2 mg/kg/d TMP). These antibiotics are generally associated with fewer adverse events, lower risk of developing multidrug-resistant secondary infections, do not disrupt commensal gut flora, and are affordable. CAP should be stopped or altered if a resistant microorganism is identified in the urine culture of a pediatric patient, even if contamination of the urine culture is suspected. In a paediatric patient with spina bifida and neurogenic bladder, intravesicular irrigation with aminoglycoside may be used for treatment and prophylaxis of UTIs, but there are no data on long-term toxicity in paediatric patients (ALSUBAIE; BARRY, 2019).

CONCLUSION

Urinary tract infections (UTIs) in children present a significant concern in pediatric practice, requiring careful attention to diagnosis and treatment. The variability in the incidence of UTIs based on age and sex, along with the diversity of pathogens involved, underlines the importance of personalized approaches to the management of these infections. Effective therapy, especially in cases of neonates and infants, is crucial to avoid serious complications such as urosepsis and kidney scarring.

The choice of antibiotics should be based on local patterns of antimicrobial susceptibility and the results of urine cultures, ensuring the use of appropriate agents for treatment. In addition, continuous antibiotic prophylaxis (CAP) plays an important role in preventing recurrent UTIs in children with anatomical abnormalities of the urinary tract, although its use should be carefully monitored and adjusted as needed.

Preventive measures, including proper hygiene and judicious administration of antibiotics, are essential to reduce the occurrence of UTIs and improve the quality of life of affected children. Comprehensive management of UTIs in children requires an integrated approach, including both therapeutic and preventive strategies, in order to minimize long-term complications and promote pediatric health and well-being

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