

## Urinary Tract Infection in Pediatrics: Clinical Approach and Follow Up

### Infecciones del tracto urinario en pediatría: enfoque clínico y seguimiento

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#### Abstract

*Urinary tract infection (UTI) is a frequent pathology in the pediatric age, about 5-8% of children under 2 years of age with fever without defined focus have a UTI, it is a frequent infection, and although most cases have good prognoses, it will always be necessary to identify those patients at risk of permanent and progressive kidney damage. UTI has a high incidence during childhood, appearing in about 7% of febrile children under one year of age and is an indicator of anatomical and functional anomalies. Clinical suspicion will always be important to reach a rapid diagnosis, in order to perform timely treatments and thus reduce kidney damage and complications. In this article we make a particular emphasis on the clinical approach and the follow-up that should be done to a patient with this pathology.*

**Keywords:** Urinary infection, Pediatrics, diagnosis, monitoring and clinical approach

#### Resumen

*La infección del tracto urinario (ITU) es una patología frecuente en la edad pediátrica, alrededor del 5-8% de niños menores de 2 años con fiebre sin foco definido tienen una ITU, es una infección frecuente, y aunque la mayoría tienen un buen pronóstico, siempre será necesario identificar aquellos pacientes con riesgo de daño renal permanente y progresivo. La ITU tiene una alta incidencia durante la infancia apareciendo en cerca de 7% de los niños febriles menores de un año y es un indicador de anomalías anatómicas y funcionales. Siempre será importante la sospecha clínica para llegar a un diagnóstico rápido; con el fin de realizar tratamientos oportunos y de esta manera reducir el daño renal y las complicaciones. En este artículo hacemos un particular énfasis en el enfoque clínico y el seguimiento que se le debe realizar a un paciente con esta patología.*

**Palabras clave:** Infección urinaria, Pediatría, diagnóstico, seguimiento y enfoque clínico.

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## INTRODUCTION

8-10% of girls and 2-3% of boys will have symptomatic UTI before the age of seven, being more frequent in males in the first three months of life and producing a progressive increase with predominance of girls from the first year of life (1).

In the first 4-6 months of age, it is more frequent in the male sex, with a boy / girl relationship with a 4/1 ratio. After 3 years, the UTI is much more frequent in girls, so that 5% of school girls suffer from it, with a girl / boy ratio greater than 10/1 (2).

UTIs are one of the most common bacterial infections, approximately 5-14% of pediatric emergencies are due to this cause (3,4).

Finally, we can say that its incidence is related to age and sex. Existing epidemiological studies are very heterogeneous, with variations between one and the other regarding the definition of UTI, the populations studied and the methodology used for the collection of the urine samples. On the other hand, children with UTI, especially the smallest ones, present a nonspecific symptomatology, which sometimes makes the UTI be undetected (5).

The UTI encompasses a heterogeneous group of conditions that their commonality is the presence of bacteria in the urine. Urinary tract infection (UTI) is defined as the invasion, colonization and bacterial proliferation of the urinary tract, which can compromise from the bladder to the renal parenchyma.

In the same way, we can classify it according to its location, presence or absence of complications, and degree of recurrence.

### Location:

#### Upper UTI:

**Acute pyelonephritis:** It is characterized by fever > 38.5 °C associated with signs of inflammation such as increased acute phase reactants such as C-reactive protein, erythrocyte sedimentation rate and is a potential risk for kidney damage with possible cortical scars (6).

#### Lower UTI:

**Cystitis:** It occurs when there is localized involvement in the urinary bladder, fever usually does not occur, with the presence of voiding symptoms such as dysuria, frequency and absence of lumbar pain. Other than that, it does not represent a risk of kidney damage (2).

**Urethritis:** it is a pathology that occurs infrequently in the pediatric age. It can be manifested in the same way with voiding symptoms without fever and, occasionally, exudate may occur, which is more frequent in adolescence. In younger children, it can be part, practically indifferent from the clinic, of balanoposthitis, or of vulvovaginitis.

According to its clinical presentation and / or renal structural damage

**Uncomplicated UTI:** characterized by absence of alteration in the structure or function of the urinary tract evidenced by imaging studies (6). These symptoms correspond to low UTI, and an uncomplicated UTI is characterized by the following:

- Febrile or fever
- Age > 2 years
- Urinary symptoms

- No toxic appearance
- No associated co-conditions
- Little or no elevation of acute phase reactants
- Complicated UTI: alteration in renal function or damage at the structural level, corresponding to high UTI, usually occurs:
  - Fever > 38.5.
  - Infants.
  - Toxic aspect.
  - Antecedents of UTI and / or associated comorbidities.
  - Leukocytosis and increased acute phase reactants.

According to its recurrence: Reinfection, relapse and recurrent.

- Reinfection: Recurrent UTI due to a germ that may be the same or another but with an interval greater than 6 weeks.
- Relapse: recurrent UTI due to the same germ but with a time interval of less than 6 weeks.
- Recurrent: defined as 3 or more episodes of low UTI or 2 or more pyelonephritis in a period of 1 year.

It is important to be clear about the definition of asymptomatic bacteriuria since it occurs very frequently and can sometimes be confusing as to the initiation or not of antibiotic therapy.

Asymptomatic bacteriuria: asymptomatic patient with absence of elevation of acute phase reactants and inflammatory markers and positive urine culture (7).

## ETIOLOGY

The etiologic agent of UTIs in Pediatrics is very similar to that of the rest of the population, however the etiological agent most frequently

isolated in UTI continues to be *Escherichia coli*, occurring in approximately 76-90% of the episodes, followed by other germs such as *Klebsiella* 0,5-8%, *Proteus* 0,5-6%, *Staphylococcus* spp. 1-5%, And *Pseudomonas* spp. 2%, which are related to some risk factors of each patient (8).

## PATHOGENY

The route of infection is almost always ascending, from microorganisms from the intestine that are found in the perineal area and ascend through the urethra to the bladder (2). Some strains of *E. coli* have adhesion factors on their surface that facilitate union to the bladder mucosa and the subsequent development of UTI.

This ability of some microorganisms to adhere to the cells of the urinary epithelium is the main factor that contributes to the initial colonization of the mucosa. Adhesion to epithelial cells occurs due to filamentous structures that are located in the capsule of bacteria called fimbrias or Pili.

Children who have an abnormality of their excretory pathways that cause an obstruction to urinary flow or a vesicoureteral reflux, have a much higher risk of infected urine reaching the kidney and causing pyelonephritis (9).

Hematogenous spread to the urinary system is a rare cause of UTI, this can occur in newborns and children with immunodeficiency. In this case the related germs are group B *Streptococcus*, *Staphylococcus aureus*, *Candida* and *Salmonella* can cause pyelonephritis through of the hematogenous route.

One of the defense mechanisms to prevent bacterial growth in the urinary tract is based

on urination itself, which leads to a continuous desquamation of the superficial epithelial cells to which the bacteria are attached. That is, the bacteria are washed out of the bladder by repeated urination and the sterility of the urine depends to a large extent on the absence of interruption of the urinary flow (5).

## PREDISPONENT FACTORS FOR UTI

Predisposing factors for the development of UTI are urinary tract anomalies that favor the slowing of the urinary flow, including VUR, phimosis in male infants, lower urinary tract dysfunction and constipation, as well as instrumentation. of the urinary tract, the neurogenic bladder and nephrourolithiasis. Some studies show the protective factor of prolonged breastfeeding for more than six months (5).

Finally, there are risk factors for the presence of permanent renal damage, such as in patients with high-grade vesicoureteral reflux and recurrent UTI. There is some evidence, but with contradictory data, in relation to the age of the patient and the delay in starting treatment as risk factors for the appearance of scars (10).

Predisposing factors for UTI in the pediatric age: White race in both sexes, Absence of breastfeeding, Male sex during the first year of life, Constipation Presence of renal anomaly, Vesicoureteral Reflux, Arterial hypertension, Pole failure UTI, Background Lip synechia Pathological phimosis Frequent bladder catheterization (4),

## CLINIC

The clinical presentation of UTI varies with age. In infants, infection is usually diagnosed later due to non-specific initial signs, such as

fever, in addition to the inability to express symptoms or localize pain. Older children can usually manifest the first symptoms of UTI, such as dysuria or abdominal pain, and therefore the infection can be identified slightly earlier than in infants (11-13).

**Table 1.** Clinic of UTI in newborns

| NEWBORNS                          |
|-----------------------------------|
| Septic table                      |
| Thermal instability               |
| Irritability / lethargy           |
| Rejection of the oral route       |
| Vomiting                          |
| Abdominal distension              |
| Jaundice                          |
| Fever isolated after the 1st week |

**Fuente:** Propia de los autores

**Table 2.** UTI clinic in children under 2 years

| INFANTS AND CHILDREN UNDER 2 YEARS OLD |
|--|
| Fever                                  |
| Vomiting                               |
| Diarrhea / constipation                |
| Abdominal pain                         |
| Hematuria                              |
| Fever                                  |

**Source:** authors

**Table 3.** Clinic UTI in schoolchildren

| LOW UTI                     |
|-----------------------------|
| Dysuria                     |
| Frequent Urination          |
| Urinary Urgency / Retention |
| Enuresis                    |
| Low grade fever             |
| Hematuria                   |

**Source:** authors.

**Table 4.** Clinic UTI in schoolchildren

| LOWER UTI                   |
|-----------------------------|
| Fever                       |
| Shaking chills              |
| Abdominal pain              |
| Vomiting                    |
| Abdominal pain              |
| Low back pain or tenderness |

Source: authors.

### UTI RISK ESTIMATION

Neonates and children younger than 24 months who present with UTI often present with fever. Fever is a common and nonspecific symptom for which physicians should consider UTI as a possible etiology, especially when there are no other obvious signs or symptoms to suggest another diagnosis.

The probability of a UTI increases as the number of risk factors, or findings, increases. The risk factors for urinary tract infection in female infants include the white race, age less than 12 months, temperature higher than or equal to 39°C and absence of another source of infection.

The probability of developing UTI in male patients is influenced by whether or not they present circumcision. In children under 24 months without circumcision, the risk of UTI without any additional risk factor exceeds 1%. The probability of UTI in infants is related to the presence of some risk factors which are presented in the following tables:

**Table 5.** Probability of UTI in female infants according to the number of findings

| PARAMETER               | VARIABLE   |
|-------------------------|--|
| Individual risk factors | White race<br>Age <12 months<br>Temperature ≥ 39 fever > 2 days<br>Absence of another infectious focus |
| Probability of UTI      |  |
| ≤ 1%                    | No. of risk factors present ≤ 1  |
| ≤ 2%                    | No. of risk factors present ≤ 1  |

Source: reference (4).

**Table 6.** Probability of UTI in male infants according to the number of findings

| PARAMETER               | FINDINGS  |
|-------------------------|---|
| Individual risk factors | FINDINGS  |
| Probability of UTI      | Non-black breed<br>Temperature ≥ 39 fever > 24 hrs<br>Absence of another infectious focus |
| ≤ 1%                    |   |
| ≤ 2%                    | No. Of risk factors present: for circumcised children ≤ 2                                 |

Source: reference (4).

### DIAGNOSIS

It is considered necessary to obtain a urine sample to confirm or rule out a suspicion of UTI, especially when there is a febrile condition without a clear focus (7,14).

We must suspect a UTI when presenting a pathological uroanalysis. This must be confirmed by the uroculture which is considered the gold standard test.

There are situations in which bacteria may be present in the urine without causing infection and inflammation, this is defined as asymptomatic bacteriuria.

In neonates and children under 24 months of age, collection of urine with a collection bag tends to be contaminated; therefore, bladder catheterization (catheter) should be used for urine sample collection for uroanalysis and urine culture. Observational studies estimate a high risk of contamination and low positive predictive value of urine cultures with a collection bag. Only those cases that the results of the uroanalysis, whose sample was taken with a collection bag when it is not pathological, should be taken into account (15).

Technique: Vesical catheterization

Advantage: It can be used for initial urine culture

Disadvantages: Pain and discomfort

Technique: Collection bag

Advantage: No discomfort and pain

Disadvantage: More time, Pathological results must be confirmed by urine culture

## INTERPRETATION OF UROANALYSIS

Urine dipstick can be used to analyze the presence of leukocyte esterase (a marker of white blood cells) and nitrites (a marker of some gram-negative bacteria). However, it does not detect the concentration of leukocytes, therefore microscopy should be used to evaluate this and other parameters, and in this way improve sensitivity. Pathological  $\geq 5$  leukocytes / field in non-centrifuged urine and  $\geq 10$  leukocytes / field in centrifuged urine is considered pathological.

The nitrite test has little sensitivity in neonates since they empty their bladders frequently, often before the required 4 hours for gram-negative bacteria to form nitrites. As such, the

absence of urinary nitrites does not rule out UTI (6). Another parameter that is currently used is the presence of bacteria in the gram of urine without centrifuge which has a sensitivity of 90.3% and a specificity of 93.5%

**Table 7.** Sensitivity and specificity of the components in the urinalysis, alone and in combination

| PARAMETER                           | SENSIVITY%    | SPECIFICITY % |
|-------------------------------------|---------------|---------------|
| Leukocyte esterase                  | 83 (67–94)    | 78 (64–92)    |
| Nitrites                            | 53 (15–82)    | 98 (90–100)   |
| Leukocyte esterase + nitrites       | 93 (90–100)   | 72 (58–91)    |
| Leukocytes by microscopy            | 73 (32–100)   | 81 (45–98)    |
| Bacteria by microscopy              | 81 (16–99)    | 83 (11–100)   |
| Leukocytes + bacteria by microscopy | 99.8 (99–100) | 70 (60–92)    |

**Source:** references (10) and (16).

## INTERPRETATION OF THE UROCULTP

The results must be interpreted carefully. Consider the number of colony forming units (CFU) per milliliter, type of bacteria species identified, and the time elapsed in processing the urine sample.

**Table 8.** Criteria of UTI in urine culture according to urine collection method

| COLLECTION METHOD       | UROCULTIVE POSITIVE                       |
|-------------------------|---|
| Clean voiding jet       | 100,000 CFU / ml of a germ                |
| Adhesive bag            | 100,000 CFU / ml of a germ                |
| Vesical catheterization | From 100,000 to 50,000 CFU / ml of a germ |
| Suprapubic puncture     | Any growth of germs                       |

**Source:** reference (9).



## COMPLEMENTARY STUDIES AT UTI

### Kidney and urinary tract ultrasound:

It should be done to all patients with febrile or afebrile UTI, it is a comfortable, non-invasive, economical method that does not emit radiation. However, this only serves to evaluate the anatomy of the urinary tract and it has no use for the diagnosis of vesicoureteral reflux, pyelonephritis and much less renal scars (16,17)

### Renal scintigraphy with DMSA:

It is the gold standard for the diagnosis of acute pyelonephritis and the presence of scars and their extension, it should be indicated when a clinical pyelonephritis is diagnosed, alterations in renal ultrasound and recurrent UTI. This should not be done at the time of infection since there is a high percentage of children under 5 years of age who are positive; for this reason, it is recommended that it be performed 4 to 6 months after the acute event with the objective of showing renal scars (18).

### Voiding cystourethrography:

It is the main imaging study for the diagnosis of vesicoureteral reflux and dysfunctional elimination syndrome. It is not recommended to perform it after 3 years of age since it is unlikely that at this age this is the cause of a first episode of UTI, and that this is secondary to vesicoureteral reflux. This study should always be performed in UTI treated with negative urine culture.

## HOSPITALIZATION CRITERIA

Regarding the management of UTIs, it is important to establish taking into account the evolution and the presence of some risk factors that patients should be treated in-hospital.

- Age less than three months
- Hydration status
- General appearance (toxic)
- UTI Background
- Anatomical alterations
- Reconsultant
- Therapeutic failure
- High social risk.

## TREATMENT

Generally, the treatment of a UTI starts before clinical suspicion and, empirically, this will depend clearly on the evolution, presence of complications and local epidemiology according to studies carried out in each institution taking into account types of isolated germs and resistance profile to antibiotic therapy (19).

**Table 9.** Empiric antibiotic therapy of first choice in uncomplicated UTI

|                |                          |
|----------------|--------------------------|
| Cephalexin     | 50 mg / kg / day -7 days |
| Nalidixic acid | 55 mg / kg / day -7 days |
| Nitrofurantoin | 7 mg / kg / day -7 days  |

Source: authors.

**Table 10.** Empiric antibiotic therapy of first choice in complicated UTI neonates younger than 4 months

|            |                                     |
|------------|-------------------------------------|
| Ampicillin | 100 mg / kg / day- 7 days (minimum) |
| Gentamicin | 5-7 mg / kg / day -7 days (minimum) |
| Amikacin   | 15 mg / kg / day - 7 days minimum   |
| Cefalotin  | 100 mg / kg / day -7 days minimum   |

Source: authors.

**Table 11.** Empiric antibiotic therapy of first choice in complicated UTI neonates older than 4 months

|             |                                     |
|-------------|-------------------------------------|
| Amikacin    | 15 mg / kg / day - 7 days minimum   |
| Gentamicin  | 5-7 mg / kg / day -7 days (minimum) |
| Cefalotin   | 100 mg / kg / day -7 days minimum   |
| Cephadrine  | 100 mg / kg / day -7 days minimum   |
| Ceftriaxone | 100 mg / kg / day -7 days minimum   |

Sources: authors.

## ANTIBIOTIC PROPHYLAXIS

### Indications:

Grade III vesicoureteral reflux, Pedal-calyceal ectasias, Neurogenic bladder, recurrent UTI, less than 2 years with febrile UTI until studies are completed.

Antibiotics for antibiotic prophylaxis: Cephalixin 15 mg / kg / day Nitrofurantoin 25 mg / kg / day Nalidixic acid 30 mg / kg / day Trimetropinsulfamethoxazole 2mg / kg / day

Antibiotic prophylaxis should be performed with 30% of the therapeutic dose at night, and should be used continuously at least until the relevant studies are done and the Etiology is clear.

### Enviar figura

Source: authors

**Figure 1.** UTI Flow chart approach

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