

Uncomplicated urinary infection in women: diagnosis

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FINAL DEVELOPMENT

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CONFLICT OF INTEREST

None.

DESCRIPTION OF THE EVIDENCE COLLECTION METHOD

The bibliographic review was carried out at MEDLINE, Cochrane and SciELO databases. Evidence search was conducted based on actual clinical scenarios and used the following keywords: (Infection, Urinary Tract OR Tract Infections, Urinary OR Urinary Tract Infection) AND Cystitis AND Risk Factor AND (Urinalyses OR Urinalysis) AND (Diagnosis, Laboratory OR Laboratory Techniques and Procedures) AND Staining and Labeling AND (Anti-Bacterial Agents OR Agents, Anti-Bacterial) AND (Diseases, Vaginal OR Vaginal Disease).

DEGREE OF RECOMMENDATION AND STRENGTH OF EVIDENCE:

- A:** Experimental or observational studies of best consistency.
- B:** Experimental or observational studies of least consistency.
- C:** Case reports (non-controlled studies).
- D:** Opinion without critical evaluation, based on consensus, physiological studies or animal models.

OBJECTIVE

To assess the main conducts in the diagnosis of urinary tract infection (UTI) in women, according to the available evidence.

INTRODUCTION

Urinary tract infection (UTI) is one of the most incident bacterial infections in adults, developing in either the low or the upper urinary tract. More than 50% of the women will have an episode of UTI throughout life¹(**D**).

Up to 15% of women develop UTIs every year and at least 25% of them will have one or more recurrences²(**B**),³(**D**). In sexually active women, the incidence of cystitis is estimated at 0.5 to 0.7 episodes per person/year⁴(**A**).

Of the pathogens involved in cystitis, *Escherichia coli* is the most frequent one, with 74.6% of the cases⁵(**B**). Other enterobacteria such as *Proteus mirabilis* and *Klebsiella pneumoniae* are accountable for approximately 4% of the cases. Of the Gram-positive bacteria, the most frequent ones are *Staphylococcus saprophyticus*, group B β -hemolytic streptococci and *Enterococcus faecalis*⁵(**B**).

Cystitis is the infection limited to the lower urinary tract with symptoms such as dysuria, polyuria and, eventually, suprapubic pain⁶(**D**). Four symptoms and a sign (including dysuria, frequency, hematuria, back pain, costovertebral angle pain) significantly increase the probability of UTI⁷(**A**). The cystitis considered complicated is the one that occurs in patients with functional or structural alteration in urinary tract or with diseases that predispose to UTI, such as diabetes or AIDS⁸(**D**). The use of urinary catheters, renal transplant and pregnancy are also considered complicated UTI criteria^{9,10}(**D**). In practice, the occurrence in any patient that is not a young, healthy and non-pregnant female, from the community, is considered a complicated cystitis. The differentiation between complicated and non-complicated cystitis is vital, due to the aspects related to clinical evolution and the choice and duration of antibiotic therapy¹⁰(**D**). Acute pyelonephritis is an infection of the kidney parenchyma and the pyelocaliceal system accompanied by significant bacteriuria, generally presenting with fever, lumbar pain and chills^{6,10}(**D**).

In young women, the most important risk factors for cystitis are recent or frequent sexual activity, use of nonoxinol-9 spermicide (including condoms) and an antecedent of UTI³(**D**),⁴(**A**). Other factors that increase the risk of cystitis are changes in the vaginal flora due to menopause and use of antibiotics and bladder emptying alterations due to cystocele or uterine prolapse¹¹(**D**).

1. ARE THE HISTORY AND PHYSICAL EXAMINATION ENOUGH FOR THE CLINICAL DIAGNOSIS IN WOMEN WITH UNCOMPLICATED CYSTITIS?

Symptoms of uncomplicated infection in the lower urinary tract are frequent complaints of women that seek emergency medical assistance. The assessment of the clinical picture, evaluated through clinical history and physical examination is an adequate indication of the possibility of acute uncomplicated cystitis. The inclusion of additional diagnostic tests can reinforce the safety of the diagnosis.

When assessing a population of women with a mean age of 28 years, non-pregnant and without clinical pathologies, with a prevalence of UTI of around 28% and symptoms of urinary frequency and/or dysuria, without vaginal symptoms (leucorrhea or vaginitis), present in the last three months and who had not received antibiotic therapy in the last four weeks, we observed that, by associating the complaints of dysuria, urinary frequency and urgency, there is a possibility of UTI > 90%^{12,13}(B).

Therefore, one can observe that the assessment of specific symptoms, such as the presence of dysuria, urinary frequency and urgency and absence of vaginitis symptoms, evaluated through clinical history, result in a correct diagnosis of UTI in more than 90% of the cases.

RECOMMENDATION

Clinical symptoms, characterized by urinary frequency, dysuria and urinary urgency, when present in association and in the absence of symptoms of vaginitis, determine an increase in the possibility of a UTI episode, considering the elevated pre-test probability.

2. WHAT IS THE SENSITIVITY AND SPECIFICITY OF THE URINE DIPSTICK TEST FOR THE DIAGNOSIS OF URINARY TRACT INFECTION IN SYMPTOMATIC WOMEN?

When assessing a urine sample (through a dipstick test or urine culture) in non-pregnant women with a mean age of 43 years (SD = ± 17 years) and complaints of dysuria, urinary urgency and frequency, with a temperature < 38°C, it was observed that the positive predictive value (PPV) for the nitrite test was around 96%, with specificity of 94%¹⁴(B). Regarding the negative predictive value (NPV) and sensitivity, we observed, respectively, 30% and 44%. In cases where the nitrite test was negative, the PPV for the leukoesterase test is around 79% with a sensitivity of 82%¹⁴(B). However, when both the nitrite and the leukoesterase tests are negative, in approximately half the cases the urine culture (≥ 10³ CFU/mL from midstream urine specimen) shows to be positive¹⁴(B). In other words, a negative dipstick test does not rule out the possibility of UTI.

RECOMMENDATION

In women with complaints of dysuria, polyuria and urinary urgency, a positive nitrite test or negative nitrite test with positive leukoesterase test are indications of UTI. However, when both tests are negative, one cannot rule out the possibility of infection.

3. HOW IMPORTANT IS TO USE URINE SAMPLE ANALYSIS (URINALYSIS, TYPE I URINE, ABNORMAL AND SEDIMENTAL ELEMENTS (ASE), ROUTINE, URINE SUMMARY, BIOCHEMICAL ANALYSIS AND SEDIMENTS) FOR THE DIAGNOSIS OF UTI IN WOMEN?

The routine urinalysis basically consists of the physical

analysis, chemical analysis and microscopic assessment. The analysis of urine to assess leukocyturia and bacteriuria can be performed by conventional techniques, with the microscopic assessment of centrifuged urine. Although Kass¹⁵(D) defined a value of 5 leukocytes/field at a magnification of 40x, this test has low reproducibility, sensitivity, specificity and PPV, identifying only 30% to 50% of the UTI cases. On the other hand, the technique of hemocytometer count chamber technique for the analysis of non-centrifuged urine has a sensitivity of 96% in the identification of symptomatic adults with UTI, using as pyuria a value ≥ 10 leukocytes/mm³¹⁶(D).

In women with dysuria, polyuria and absence of vaginal discharge, it is not necessary to perform the urine analysis and empiric treatment can be started. If the history is not a typical one, then a dipstick test can be performed. A positive result for leukocytes or nitrite is correlated with a probability of 80% of UTI. However, a negative result does not rule out the probability of UTI, and then, urine culture and clinical follow-up are recommended¹⁷(B).

RECOMMENDATION

Urine analysis is not necessary for the diagnosis of urinary infection in women with symptoms of dysuria, polyuria and no vaginal discharge. The negative urine analysis result does not rule out the probability of UTI, which must be investigated by urine culture.

4. WHEN IS THE URINE CULTURE INDICATED IN WOMEN WITH A CLINICAL PICTURE OF CYSTITIS?

Although acute cystitis represents a very frequent type of infection in women, there are several diagnostic tests for this disorder^{1,3}(D),¹⁸(C). As the diagnosis of cystitis can be carried out through the clinical history alone, the request for additional tests must be made by the assistant physician whenever he or she deems necessary.

Even though cystitis represents a frequent cause of dysuria, other disorders can present the same symptomatology such as urethritis, caused by *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and vaginitis caused by species of *Candida* or *Trichomonas vaginalis*. Due to this similarity, the presence of other symptoms, such as urinary frequency and urgency and hematuria, evaluated through the clinical history, increase the probability of a lower UTI, thus being a useful strategy for the diagnosis of cystitis¹³(B).

However, women with a clinical picture of complicated cystitis, represented by BT > 38°C, symptoms of abdominal pain, nausea, vomiting, chronic urologic or kidney abnormalities, immunosuppression, *diabetes mellitus* or an atypical clinical picture, need additional assessment, carried out by diagnostic tests that include urine culture and antimicrobial susceptibility test¹⁹(D).

RECOMMENDATION

In women with no risk factors for complicated UTI or vaginal complaints and symptoms of dysuria and polyuria, there is a high probability of cystitis, and it is not necessary to request additional tests to institute treatment.

5. IS THERE INDICATION FOR URINE CULTURE AFTER THE TREATMENT? WHEN AND IN WHICH SITUATIONS?

A control urine culture is unnecessary in healthy women, as the results are almost 100% negative and the relative risk of a subsequent UTI is equivalent to that of women that did not have the test²⁰(B). In cases with persistent or recurring symptoms, the culture must be carried out²¹(A).

RECOMMENDATION

It is not necessary to perform a urine culture after the treatment with symptom resolution in healthy women.

6. WHAT IS THE ROLE OF IMAGING ASSESSMENT IN WOMEN WITH UNCOMPLICATED CYSTITIS?

The diagnosis of UTI is primarily based on symptomatology, associated or not with additional tests²²(D). The approach of uncomplicated infection in the lower urinary tract in women generally does not require radiological assessment, as the frequency of anatomic lesions that can be corrected is very low. In general, the request of an imaging assessment must be reserved for cases with therapeutic failure or those with severe or recurrent symptomatology, being also requested in cases where it is necessary to differentiate upper from lower urinary tract infection²³(D).

RECOMMENDATION

The diagnosis of UTI remains predominantly a clinical one. The main role of the imaging assessment is to promote the investigation of patients with recurrent and unusual manifestations.

7. WHAT IS THE IMPORTANCE OF THE CLINICAL HISTORY AND PHYSICAL EXAMINATION IN THE DIFFERENTIAL DIAGNOSIS BETWEEN UPPER AND LOWER URINARY TRACT INFECTION?

The diagnosis of upper UTI (pyelonephritis) in some circumstances, can be carried out through invasive tests, such as the excretion urography or through imaging assessment tests such as ultrasonography²⁴(D). However, in clinical practice, the clinical history and the physical examination have important roles. When retrospectively assessing women with a mean age of 35 years (SD = ± 18.3) with a diagnosis of UTI (attained through leukocyte count in urine specimen ≥ 7 in high-magnification field), it was observed that among the symptoms consistent with pyelonephritis such as nausea, vomiting, painful fist-percussion test, presence of fever $> 37.8^\circ\text{C}$ increased the probability from 7% to

35% ($p = 0.02$)²⁵(B). The presence of BT $\geq 37.8^\circ\text{C}$ associated with a suggestive clinical picture of UTI has a PPV of 98%, compared with 84% in the absence of fever²⁵(B).

RECOMMENDATION

The presence of the fever criterion (BT $\geq 37.8^\circ\text{C}$) associated with signs and symptoms suggestive of upper UTI have a high PPV for pyelonephritis (upper UTI). Cases suspected of having upper UTI with suggestive signs and symptoms, but no fever, must be assessed for diagnostic alternatives.

8. DOES THE URINE BACTERIOSCOPY (GRAM'S METHOD) HAVE DIAGNOSTIC AND PROGNOSTIC VALUE?

Bacteriuria can be detected microscopically through Gram's method in urine samples that have not been centrifuged or by the direct observation of bacteria in the sample. The test performance is yet to be fully established, as different criteria have been used to define a positive result²⁶(C).

The bacterioscopy of urine using Gram's method has the important advantage of providing prompt and relevant information regarding the nature of the UTI agent, thus facilitating the empiric selection of the antibiotic to be used. However, the disadvantage is a decrease in sensitivity, being reliable only in urine samples with concentrations of bacteria $> 10^5$ CFU/mL. Concentrations of bacteria between 10^2 and 10^3 CFU/mL, might go undetected by this test, in addition to the amount of time necessary for it to be performed, which prevents its routine use²⁷(D).

Due to such limitations, such test must be carried out in patients with a clinical picture compatible with that of acute pyelonephritis, severe UTI and other situations where it is important to have immediate information on the type of bacteria is involved.

RECOMMENDATION

Urine bacterioscopy using Gram's method is a test with reduced sensitivity, but has the advantage of allowing the identification of the UTI agent. Therefore, it can indicate the empiric treatment in patients with acute pyelonephritis or others, where the information on the type of bacteria involved is important.

9. DOES THE RESULT OF LEUKOCYTE COUNT IN URINE INDICATE THE SEVERITY OF THE DISEASE IN WOMEN WITH UTI SYMPTOMS?

Leukocyturia is not a specific finding of UTI, being also present in tumors, kidney stones, use of certain drugs (cyclophosphamide, for instance) and contamination by vaginal secretions. In samples with very low density or high pH, the leukocytes can undergo rupture and might escape observation at the microscopy. Therefore, the determination of leukocyte esterase, a leukocyte-specific protein,

can have a higher degree of correlation with bacteriuria than the microscopic analysis of urinary sediment²⁷(D).

On the other hand, the leukocyte count can indicate the cystitis response to treatment. In cases with a favorable evolution, values return to normal in 2 to 7 days; however, in those without therapeutic response, the leukocyturia persists²⁸(C).

RECOMMENDATION

The amount of leukocytes at the microscopy does not have diagnostic value, but reflects the therapeutic response to the UTI treatment.

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