Validity of Urine and Blood Tests for Detection of Urinary Tract Infections in Children

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Abstract

Objective: The goal was to provide a prospective comparison and determine the validity of urine and blood tests for detection of urinary tract infections (UTIs) in young children.

Material and Methods: The study population consisted of a random sample of children 0.5-12 years of age who presented to the Education and Research Hospital of Recep Tayyip Erdoğan University with symptoms suggesting UTIs. Urine samples were obtained from every child by urinary bag collection or clean catch as appropriate for age. Urine specimens underwent four tests simultaneously: nitrite, leukocyte esterase, urinalysis (microscopic), and urine culture. Complete blood count and C-reactive protein (CRP) of participants were tested in blood samples.

Results: A total of 327 children were included in the study; 45.5% of boys and 31.4% of girls had a positive urine culture result, and 30.4% of assessed urine samples were evaluated as contamination. Based on the study, the most sensitive test for the diagnosis of UTI was microscopy, and the most specific test for the diagnosis of UTIs was nitrite.

Conclusion: According to the findings obtained from the study, microscopy should be considered as a basic test with culture, but the results of microscopy must be supported by other tests, especially nitrite. CRP is unlikely to be a good parameter for the screening of UTIs according to the study.

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Introduction

Urinary tract infections (UTIs) are the most common cause of serious infections among young children (1-3). The epidemiology of UTIs varies by age, gender, and other factors. The incidence of UTIs is highest in the first year of life for all children (4). Urinary tract infections may result in long-term sequelae, including renal scarring and hypertension (5, 6). It is imperative that physicians identify these children to institute early treatment (7). Diagnosing UTIs has been the focus of many studies over the past 60 years (8). Although urine obtained by suprapubic aspirate (SPA) or transurethral catheter in young children is the preferred specimen for documenting UTIs, these methods can not be applied at all times in outpatients. This situation increases the importance of screening tests (9). Although there are several screening tests for UTIs, there have been rare prospective clinical comparisons of these tests in contaminated samples in the literature. The purpose of the present study was to provide a prospective comparison and determine the validity of urine (leukocyte esterase, nitrites, microscopy, and urine culture) and blood (complete blood count (CBC), C-reactive protein (CRP) tests for the detection of UTIs in young children.

Material and Methods

The study population consisted of a random sample of children 6 months to 12 years of age who presented to the Education and Research Hospital of Recep Tayyip Erdoğan University with symptoms suggesting UTIs. Inclusion crite-

ria were, for infants: fever with no apparent source, vomiting, and irritability; for toddlers: abdominal pain and voiding frequency with or without fever; and for older children: dysuria, frequency, urgency, and abdominal pain with or without fever. Children receiving antibiotic therapy were excluded from the study. Urine was cultured if the dipstick or microscopy tests were abnormal or if UTIs were clinically suspected. Age, sex, and temperature were recorded for each participant. In the study, the diagnosis of UTIs was based on a positive urine culture in patients with suggestive UTI symptoms. Urine samples were obtained from every child by urinary bag collection or clean catch as appropriate for age. In the study, there was no suprapubic aspiration sample, because suprapubic aspiration is not routinely performed in our clinic. Urine specimens went to the laboratory for analysis within 15 minutes. Also, blood samples were studied within 30 minutes. Urine microscopy specimens and cultures were processed by standard bacteriologic techniques in the laboratories of the Education and Research Hospital of Recep Tayyip Erdoğan University.

Nitrite and Leukocyte Esterase

An aliquot of non-centrifuged urine was tested for the presence of nitrite or leukocyte esterase with a fully automated urine analyzer (Arkray Aution Max Ax-4280, Iris Diagnostics) according to the manufacturer's instructions.

Complete Blood Count, C-reactive Protein

Complete blood count of participants was tested with a cell counter system (Abbott Cell-Dyn 3700 hematology analyzer) according to the manufacturer's instructions.

C-reactive protein was tested with the Immunochemistry System (Beckman Coulter Immunochemistry System, Immage 800, USA)

Urine Culture

Urine received in sterile containers or urine bags was inoculated onto blood and Eosin Methylen-blue (EMB) agar plates with a 0.01-mL calibrated loop, incubated at 35°C, and examined daily for growth for 2 days. A positive result was defined as 105 CFU/mL for urine collected from a clean catch or urine bag. The presence of three or more different organisms in a urine culture was evaluated as contamination.

Urine Microscopy

Microscopy was done by a hemocytometer on uncentrifuged urine.

Statistical Analysis

The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for the seven screening methods were calculated against the urine culture (reference group) for the diagnosis of UTIs. Sensitivity measures the proportion of actual positives that are correctly identified. Specificity measures the proportion of negatives that are correctly identified. NPV is the proportion of subjects with a negative test result who are correctly diagnosed and is used to describe the performance of a diagnostic testing procedure. PPV is the proportion of subjects with positive test results who are correctly diagnosed. It is a critical measure of the performance of a diagnostic method.

Results

A total of 327 children were included in the study: 228 girls (69.7%) and 99 boys (30.3%) (Figure 1); 45.5% of boys and 31.4% of girls had a positive urine culture result. While the rate of positive culture was 35.7%, the contamination rate was 30.4% in our study. Most of the children were from the younger age group (Figure 2). Of the cultures, 51 were positive for *Escherichia coli*, 21 were positive for *Enterococcus*, 15 were positive for *Klebsiella*, 12 were positive for *Proteus*, 9 were positive for coagulase-negative *Staphylococcus,* 3 were positive for *Pseudomonas,* and 3 were positive for *Candida albicans*. Table 1 compares the findings for the urine cultures and for the six screening tests for the diagnosis of UTIs. While the most sensitive test for the diagnosis of UTIs was microscopy, the most specific test for the diagnosis of UTIs was nitrite. Sensitivity, specificity, PPV, NPV, and accuracy values of the tests are demonstrated in Table 2.

Discussion

The original reference standard for diagnosing UTIs was the presence of significant bacteriuria, defined as the isolation of at least 10^5 colony-forming units (CFU) of a single uropathogen, in a clean catch or catheterized urine specimen (10). Unfortunately, this is not always possible, especially in outpatients. For this reason, the screening of UTIs is very important in certain countries that have too many patients per doctor. Sometimes, doctors can not have a chance to correlate the results of the urine culture with the patient's clinical status, especially in ambulatory patients. To provide better insight, this study focused on the validity and accuracy of urine screening tests in children presenting to the department of pediatrics with symptoms suggestive of UTIs. In studies, the results are usually evaluated only by positive culture, but in our study, we interpreted the results with positive culture and contamination, thinking of the possibility of certain urinary tract infections in some patients

Table 1. Results of urine cultures and screening tests

Urine Culture	WBC	CRP	Microscopy	Esterase	Nitrite	Temperature
	P N	P N	P N	P N	P N	P N
Positive	57.9%	26.3%	82.5%	52.6%	20.6%	39.1%
	42.1%	73.7%	17.5%	47.4%	79.4%	60.9%
Negative	27.8%	25.0%	14.9%	19.4%	0.0%	54.2%
	72.2%	75.0%	85.1%	80.6%	100%	45.8%
Contamination	56.3%	25.0%	46.2%	40.6%	2.3%	46.8%
	43.8%	75.0%	53.8%	59.4%	97.7%	53.2%

WBC: White blood cells; CRP: C-reactive protein; Microscopy: hemacytometer cell count (≥10/mm^3); P: positive; N: negative

Table 2. Sensitivity, specificity, PPV, NPV and accuracy values of tests

Test	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
WBC	57%	72%	68%	62%	64%
CRP	26%	75%	52%	49%	50%
Microscopy	82%	85%	86%	81%	83%
Esterase	52%	80%	74%	61%	66%
Nitrite	20%	100%	100%	55%	60%
Temperature	39%	45%	40%	44%	42%

WBC: White blood cells; CRP: C-reactive protein; PPV: positive predictive value; NPV: negative predictive value

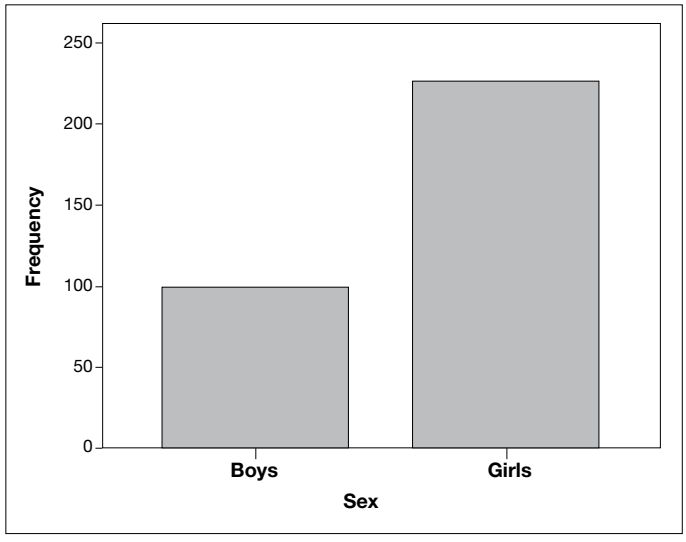

Figure 1. Gender of children

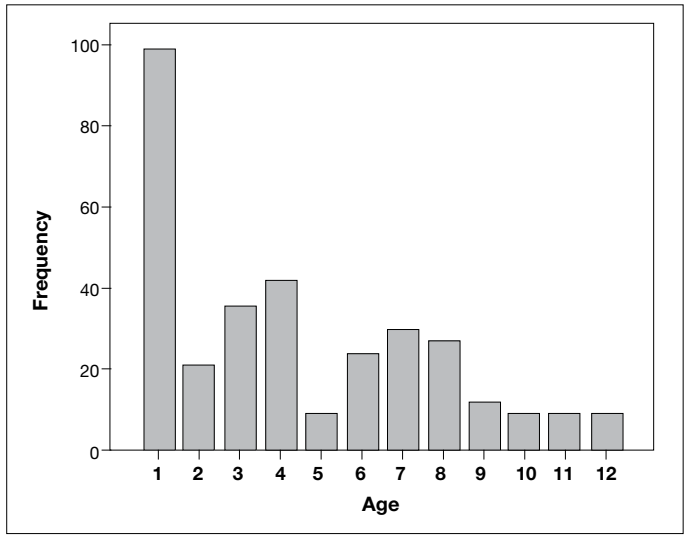

Figure 2. Age of children

of the contamination group (7, 11-13). In our study, most of the urine samples were taken with urine bags; therefore, the contamination rate may be increased, as stated by Hardy et al., but the contamination rates are still compatible with the reported rates (14, 15). While the statistical analysis showed a significant relationship between peripheral WBC, microscopy, esterase, nitrite, and positive urine culture, a statistical relationship was not found between CRP and temperature in our study (chi-square, $P<0.05$). In examining the Table 1, it is understood that come patients in the contamination group had UTIs (according to the results of the microscopy and nitrite). In such cases, if empirical treatment is planned, positivity of microscopy and nitrite can help in differentiating infection and contamination in empirical treatment planning, according to our study, because microscopy had the highest sensitivity and high specificity, PPV, NPV, and accuracy in our study. Another important finding in the study is that nitrite had the poorest sensitivity but the highest specificity. The microscopy results in our study were similar to the results of the Emergency Department of Schneider

Children's Medical Center (13). The sensitivity of microscopy for the diagnosis of UTIs in children has been reported to be in the range of 57% to 92% among studies (4). Gram-negative bacteria reduce nitrate to nitrites, and these bacteria are the most frequent cause of UTIs; therefore, the nitrite test is often found in the rapid test. The sensitivity of nitrite in our study was determined as 20%. The sensitivity range of nitrite has been reported among studies as 16%–72%; this value is compatible with our result (3, 4). Demonstration of significant pyuria is important to differentiate infections from colonization and contamination. Moreover, pyuria with UTİ symptoms, in the absence of bacterial growth on routine laboratory media, suggests an infection caused by fastidious bacteria (16). Pyuria is easily detected by a positive test for leukocyte esterase activity. When dipstick results are compared with microscopy, false-negative results by microscopy are more frequent than false-positive results by dipstick (17). In addition, false-negative results for leukocyte esterase may be due to heavy proteinuria and insufficient release of esterase from WBCs (18). The sensitivity range of leukocyte esterase has been reported among studies as 64%–89% (4). The sensitivity of leukocyte esterase in the screening of UTIs in our study was determined as 52%. This value is lower than the values mentioned above. We think that this situation may be due to the delay of transfer of samples to the laboratory (within the range specified in the method). Galloway et al. (19) suggested that serial measurement of CRP in patients with spinal injury may help distinguish between urinary tract colonization and infection; Andersson et al. (20) reported in their study that urinary level of CRP seems to distinguish between children with UTIs and other febrile conditions (19, 20). Considering the helpful guidance of indirect tests of inflammation (WBC, CRP) in the screening of UTİ, peripheral WBC and CRP were tested. As shown in the table, the positivity rate of peripheral WBC and CRP in contamination was similar with culture-positive samples (6, 21).

Conclusion

The present study provides evidence to support that microscopy is essential in the screening of UTIs, but the results of microscopy must be supported by other tests, especially nitrite; if it is positive, it will be a good supporter, with its high specificity for the diagnosis of UTIs in children. On the other hand, microscopy should be evaluated with the esterase result for differentiating infection from colonization and contamination. Finally, according to the present study, CRP is unlikely to be a good parameter for the screening of UTIs.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Medical Faculty of Recep Tayyip Erdoğan University (No: 15, 2011).

Informed Consent: Written informed consent was obtained from the patients and their parents who participated in this study.

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