Paediatrica Indonesiana

VOLUME 51 September • 2011 NUMBER 5

Original Article

Diagnostic tests of microscopic and urine dipstick examination in children with urinary tract infection

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Abstract

Background Urinary tract infection (UTI) is common in children and, if incorrectly handled, may cause long-term complications, such as renal failure. The best test to diagnose UTIs is urine culture. However, urine culture is time-consuming, taking 3 – 5 days. Therefore, there is a need for faster, alternative methods. Urinalysis is a common diagnostic test to establish the diagnosis of UTI.

Objective This study aims to determine the sensitivity and specificity of urine leukocytes, nitrite and leukocyte esterase for UTI diagnosis.

Methods We performed diagnostic tests at Dr Sardjito Hospital, Yogyakarta. We examined the presence of leukocytes in urine by microscopy, urinary nitrite and leukocyte esterase by dipstick test, while comparing to urine culture as the gold standard.

Results Two-hundred children were included in our study. By parallel test analysis, we found the sensitivity, specificity, positive predictive value and negative predictive value of using all 3 tests in combination were 95%, 59%, 74% and 89%, respectively.

Conclusion Tests for urine leukocytes, nitrite and leukocyte esterase have high sensitivity but low specificity for diagnosing UTIs. Therefore, negative results in these 3 tests do not rule out the possibility of UTI in children. **[Paediatr Indones. 2011;51:252-5]**.

Keywords: *urinary tract infection, urine dipstick, urine microscopic, urine culture*

Urinary tract infection (UTI) is a major health problem, particularly in children. Information on UTIs in children remains controversial and leaves many unanswered questions.[1] UTI symptoms in children are not typical or specific, making it difficult for physicians to make a proper diagnosis. However, UTIs require prompt and proper management to avoid significant future complications, such as renal scarring or kidney failure. Furthermore, UTI with complication is the cause of urosepsis, the major cause of sepsis after respiratory tract infections.[2]

Clinicians usually require laboratory examinations to confirm a UTI diagnosis. To select laboratory tests, one must consider two issues. First, a false negative test may result in increased risk of serious complications. Second, a false positive test could be costly, as it could lead to administration of unnecessary antibiotic therapy, which may give rise to microbial resistance.[3,4] The gold standard examination for UTI is urine culture. However, its main weakness is that it takes 3-5 days to obtain a result. UTI diagnosis should be rapid, so that

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proper treatment can be given promptly. Alternative methods to diagnose UTIs by urinalysis are microscopic urine examination (urine leukocytes), and urine test strips (urine nitrite and leukocyte esterase).[1] While urinalysis is readily available, relatively inexpensive, as well as fast and simple, studies have reported varying results. This study aims to determine sensitivity and specificity of urine leukocytes, nitrite and leukocyte esterase in the diagnosis of UTI.

Methods

We performed a cross-sectional study (January-December 2009) to determine the diagnostic value of urine leukocytes, nitrite and leukocyte esterase tests from suspected UTI patients, comparing to urine culture as the gold standard.[5] Subjects were obtained by consecutive sampling and included 200 children with possible UTI, aged 2 months - 18 years. Subjects were treated in Dr Sardjito Hospital as inpatients or outpatients. Criteria for clinical UTI diagnosis varied according to age group. For infants, the criteria were non-specific symptoms such as vomiting and/or diarrhea, anorexia, irritability, fussiness, fever of unknown cause, late onset jaundice in the presence of elevated levels of bilirubin (direct or indirect), and failure to thrive. For pre-schoolers, the criteria were dysuria, urgency, frequency, unusual urine smell, fever, failure to thrive, and abdominal or pelvic pain. For school-aged children, dysuria, frequency, fever, unusually foul-smelling urine, vomiting, anorexia, and abdominal pain. We excluded children who had already received antibiotics or vitamin C, and those who had glucosuria, proteinuria, urine of specific gravity > 0.030 or pH <5 and patients or families who refused to participate.

Based on UTI prevalence data, we calculated the minimum sample size required in our study to be 200 subjects. Urinalysis was performed in the Department of Clinical Pathology, Dr Sardjito Hospital. Urine specimens were collected by obtaining mid-stream urine. Examination of leukocytes in urine was performed by centrifugation followed by microscopy and counting of cells by Neubauer haemocytometer. Leukocytes were reported per high power field (HPF) and considered positive for UTI if the number of leukocyte cells was ≥ 5 cells/HPF. Dipstick urine test was used to measure levels of nitrites and leukocyte esterase visually, and the results compared with the reference colours on the box. Any colour change indicated a positive result for UTI. Urine culture was performed with MacConkey and CLED agar, with cultures incubated at 37°C and examined after 24-48 hours. The number of bacterial colonies was counted. Positive UTI was indicated by presence of bacteria ≥ 10^5 cfu/ml.

Laboratory examinations were performed by two analysts, with kappa value of 0.62, indicating agreement. This study was approved by the Medical Ethics Committee of Gadjah Mada University.

Subjects were collected by consecutive sampling, and a descriptive analysis was performed on subject characteristics and diagnostic test results (urine leukocytes, nitrite and leukocyte esterase) combined, compared to urine culture as the gold standard. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR +) and negative likelihood ratio (LR -) were then computed.

Results

Two hundred eligible subjects were included in this study. Baseline characteristics collected were age, sex, circumcised state for males, and clinical symptoms associated with UTI. **(Table 1)**

Table 1. Characteristics of subjects suspected of having UTIs

Characteristic	n = 200	Percentage, %
Age		
2 mo – 1 yr	50	25
>1 – 5 yrs	69	35
>5 – 10 yrs	45	22
>10 – 18 yrs	36	18
Gender		
Boy	65	33
Girl	135	67
Circumcised state (boys)		
Circumcised	22	34
Not circumcised	43	66
Symptoms		
Fever	102	51
Abdominal Pain	59	30
Vomiting	48	24
Dysuria	28	14
Frequency	15	8
Urgency	9	4
Enuresis	9	4
Constipation	8	3
Icterus	4	2
Positive Urine Culture	95	48

Table 2. Microbes causing UTI

Microbes	n	Percentage
Escherichia coli	38	40
Pseudomonas aeruginosa	29	31
Coagulase-negative Staphylococcus	13	14
Klebsiella pneumoniae	8	8
Citrobacter sp	3	3
Proteus vulgaris	2	2
Candida sp	2	2
Total	95	100

Discussion

Dicknson estimated the risk of UTIs in boys aged 2-14 years to be 1.6/1000/year, while in girls they found the risk to be 3.8/1000/year.[6] Of the children suspected to have UTIs in our study, the largest age group was 1-5 years old. There were more females than males and the majority of males were uncircumcised.

Table 3. Single parameter diagnostic test results

Results	Urine leukocytes	Urine nitrites	Urine leukocyte esterase
Sensitivity, %	87 (95% CI 81 to 94)	40 (95% CI 30 to 50)	88 (95% CI 82 to 95)
Specificity, %	26 (95% CI 17 to 34)	81 (95% CI 73 to 88)	30 (95% CI 21 to 38)
PPV, %	52 (95% CI 44 to 59)	66 (95% CI 53 to 78)	53 (95% CI 45 to 61)
NPV, %	69 (95% CI 55 to 84)	60 (95% CI 52 to 68)	74 (95% CI 61 to 87)
LR (+)	1.18 (95% CI 1.03 to 1.35)	2.10 (95% CI 1.32 to 3.34)	1.25 (95% CI 1.09 to 1.45)
LR (-)	0.49 (95% CI 0.26 to 0.91)	0.74(95% CI 0.61 to 0.90)	0.39 (95% CI 0.21 to 0.74)

The most common pathogen causing UTI was *Escherichia coli* (38%), followed by *Pseudomonas aeruginosa* (29%). Other pathogens were coagulase-negative *Staphylococcus, Klebsiella pneumonia*, *Citrobacter sp*, *Proteus vulgaris*, and *Candida sp* (13%, 8%, 3%, 2% and 2%, respectively). **(Table 2)**

For single parameter diagnostic test analysis, leukocyte esterase had the highest sensitivity of 88% (95% CI: 82 to 95) with specificity of 30% (95% CI: 21 to 38). Urine leukocytes had sensitivity of 87% (95% CI: 81 to 94) and specificity of 26% (95% CI: 17 to 34). Urine nitrite test had the lowest sensitivity of 40% (95% CI: 30 to 50), but showed the highest specificity of 81% (95% CI: 7 to 88) compared to other diagnostic tests. **(Table 3)**

The parallel test analysis with the combination of 3 parameters, (urine leukocytes, nitrite and leukocyte esterase) is shown in **Table 4**. This combination increased the sensitivity to 95% (95% CI: 87 to 100) and specificity to 59% (95% CI: 41 to 77).

Table 4. Parallel analysis of diagnostic tests based on three parameters

Urine leukocytes + nitrites + leukocyte esterase	Value
Sensitivity, %	95 (95% CI 87 to 100)
Specificity, %	59 (95% CI 41 to 77)
PPV, %	74 (95% CI 62 to 87)
NPV, %	89 (95% CI 76 to 100)
LR (+)	2.29 (95% CI 1.47 to 3.55)
LR (-)	0.09 (95% CI 0.02 to 0.37)

Clinical symptoms of UTI are non-specific and in some patients even occur without symptoms. However, the most common complaint of our subjects was fever. In lower UTIs, patients usually complain of pain or burning sensation in the urethra during urination with small amount of urine excreted and discomfort in the suprapubic region. In upper UTIs, symptoms of headache, malaise, nausea, vomiting, fever, chills, and/or flank pain can be found. In neonates, the symptoms are not typical so UTIs often manifest as symptoms of sepsis. Symptoms in newborns may include jaundice, pallor, cyanosis, respiratory distress, decreased appetite, decreased body weight, diarrhea, and central nervous system symptoms such as anxiety, seizures, and hypotonia. Symptoms are more specific in older children.[1,7] Rehman *et al.* documented clinical symptoms of UTI to include fever (91%), dysuria (65%), failure to grow (40%), vomiting (28%), and abdominal pain (22%).[7] We also found that fever was the most common complaint (51%) in our study subjects.

Prais *et al*. suggested that most common causes of UTIs were *E. coli* (86%,) followed by *Klebsiella sp* (6%) and other pathogens (8%).[8] Waisman *et al*. found the most common bacterial pathogens to be *E. coli* (77.3%), followed by *Pseudomonas*, *enterococcus*, and *Klebsiella* (5.7% for each) and group B *Streptococcus* and coagulase-negative *Staphylococcus* (2.8% each).[9] Other studies also reported *E. coli* to be the most common cause of UTI. Similarly, we found *E. coli*

was the most common cause of UTIs in our subjects (40%).

In previous studies, the diagnostic tests of urinalysis vary according to the research settings. For urine nitrite, Rehmani found the sensitivity, specificity, NPV, and PPV was 81%, 87%, 73%, and 91%, respectively. Leukocyte esterase had sensitivity of 77%, specificity 54%, NPV 43%, and PPV 85%.[4] For urine leukocyte test by microscopy, Simerville *et al.* found that more than 5 leukocytes per field of view had a sensitivity of 18% - 44% and a specificity of 88% - 89%, PPV 56% - 59% and NPV 83% - 95%.[10] In our study, the highest sensitivity test was urine leukocyte esterase (88%), but this test had low specificity (30%), with PPV and NPV of 53% and 74%, respectively. Furthermore, the highest specificity values were found for urine nitrite (81%), but it had low sensitivity (40%), with PPV of 66% and NPV of 60%. This result implies that there are a high proportion of patients who do not experience UTI if their urine nitrite test shows a negative result. In this study, we combined the three common parameters of urine leukocytes, nitrite and leukocyte esterase in order to increase the sensitivity and specificity of urinalysis for detecting UTIs. The combination of these three diagnostic tests improved sensitivity to 95% and specificity to 59%. PPV and NPV also increased to 74% and 89%, respectively. A study by Lohr *et al.* also documented increased sensitivity of 100% when all diagnostic tests were positive, with specificity of 66.1%.[11] We found the sensitivity to be lower than that of Lohr *et al.*, probably due to the urine not being analysed within an hour of collection, which may cause a higher rate of false positives due to contamination. This is one weakness of our study. For future studies, suprapubic aspiration is recommended to minimize the possibility of bacterial contamination.

We conclude that the combination of urine leukocytes, nitrite and leukocyte esterase tests had high sensitivity, but low specificity for diagnosing UTIs. Therefore, negative results of these 3 tests do not rule out the possibility of UTIs in children.

Acknowledgments

We would like to thank Endy Paryanto, Fita Wirastuti, Latifah Hanum, and Retno Palupi for their technical assistance.

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