Reliability of the Urinalysis for Predicting Urinary Tract Infections in Young Febrile Children

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Background: Urinary tract infections (UTIs) are a common source of bacterial infection among young febrile children. Clinical variables affecting the sensitivity of the urinalysis (UA) as a screen for UTI have not been previously investigated. The limited sensitivity of the UA for detecting a UTI requires that a urine culture be obtained in some children regardless of the UA result; however, a proper urine culture requires an invasive procedure, so the criteria for its use should be optimized.

Objectives: To determine how the sensitivity of the standard UA as a screening test for UTI varies with age, and to determine the clinical situation that necessitates the collection of a urine culture regardless of the UA result.

Methods: Retrospective medical record review of patients younger than 2 years with fever (≥38°C) seen in the emergency department during a period of 65 months. All urine cultures were reviewed for the collection method, isolates, and colony counts. A UA result was considered positive if the presence of 1 of the following was detected: leukocyte esterase, nitrite, or pyuria (≥5 white blood cells per high power field). Patients who had a paired UA and urine culture were used to calculate the sensitivity, specificity, and likelihood ratios of the UA. The prevalence of UTIs was also subcategorized by age, race, sex, and fever.

Results: Medical records of 37 450 febrile children younger than 2 years were reviewed. Forty-four percent were girls. Median age and temperature were 10.6 months and 38.8°C. A total of 11 089 patients (30%) had urine cultures obtained. The sensitivity of the UA was 82% (95% confidence interval [CI], 79%-84%) and did not vary by age subgroups. The specificity of UA was 92% (95% CI, 91%-92%). The likelihood ratios for a positive UA and negative UA were 10.6 (95% CI, 10.0-11.2) and 0.19 (95% CI, 0.18-0.20), respectively. Prevalence of UTI was 2.1% overall (2.9% for girls and 1.5% for boys, respectively). Among girls, the prevalence of UTI was 5.0% in white patients, 2.1% in Hispanic patients, and 1.0% in black patients. Among boys, the prevalence was 2.2% in Hispanic patients, 1.4% in white patients, and 0.8% in black patients. Higher prevalence was also seen among patients with a temperature at or above 39°C compared with those whose temperature was between 38.0°C and 38.9°C. The greatest prevalence of UTI (13%) was found among white girls younger than 6 months with a temperature at or greater than 39°C. The posttest probability of a UTI in the presence of a negative UA can be calculated using the negative likelihood ratio and the patient-specific prevalence of UTI. When the prevalence of UTI is 2%, 1 UA among 250 will produce a false-negative test result.

Conclusions: The sensitivity of the standard UA is 82% (95% CI, 79%-84%) and does not vary with age in febrile children younger than 2 years. The prevalence of UTI varies by age, race, sex, and temperature. A negative likelihood ratio and estimates of prevalence can be used to calculate the risk of missing a UTI due to a false-negative UA result.

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URINARY TRACT infections (UTIs) are the most common source of serious bacterial infection in young children. Overall, 3% to 5% of young febrile children have UTIs, including 5% to7% of those "without a source of fever."[1,2] Beyond the diagnosis and treatment of UTIs, the identification of a UTI in a young child prompts investigation for vesicoureteral reflux and other urinary tract anomalies that may predispose patients to long-term renal complications.[3-6] Previous publications have noted a relatively low sensitivity of the standard urinalysis (UA) for detecting UTIs in young, febrile infants.[1,7] It is common practice to obtain urine for culture in very young febrile infants who do not have an obvious source of infection and to consider a UA for older infants who do not have a focus of infection. Unfortunately, a proper urine culture requires an invasive procedure (eg, bladder catheteriza-

METHODS

Medical records were reviewed retrospectively for 65 consecutive months (January 1993 to June 1999). Children younger than 2 years with fever (temperature ≥38.0°C) who were seen in the emergency department were studied. The following variables were recorded: age, race (identified by parents), triage temperature, and laboratory test results. All urine cultures were reviewed for specimen type, colony counts, and isolates. All patients who had a paired UA and urine culture were included for calculating the sensitivity and specificity of the UA. An audit of 250 randomly selected records from our study group was performed to establish an estimate for prior antibiotic use and previously defined urologic abnormalities.

URINALYSIS

A dipstick analysis was performed for leukocyte esterase (LE) and nitrite using Multistix (Bayer Corporation, Elkhart, Ind). Degrees of LE found (1+, 2+, 3+) were all considered positive results for the presence of LE. As part of our standard UA, the laboratory performed microscopic analysis only if the dipstick indicated the presence of LE, nitrite, blood, or protein. Urine Gram stains were not routinely performed. A dipstick test result was considered positive if LE or nitrite or both were present. Pyuria was defined as greater than or equal to 5 white blood cells (WBCs) per high-power field (magnification ×40) on a spun specimen (centrifuged at 2000 rpm for 5 minutes). A positive UA result was defined as a positive dipstick test result and/or pyuria.

A urine culture was considered positive by standard criteria[8]: greater than or equal to 10^3 colony-forming units (cfu)/mL from a suprapubic aspiration, greater than or equal to 10^4 cfu/mL on catheterized specimens, and greater than or equal to 10^5 cfu/mL on clean voided specimens. Cultures were considered contaminated if more than 1 organism or nonpathogens (*Acinetobacter* species, *Candida*, *Gardnerella vaginalis*, *Micrococcus* species, *Streptococcus viridans*, *Staphylococcus nonaureus*, *Corynebacterium* species) were isolated. Cases with contaminated cultures were removed from further analysis.

RISK OF MISSING A UTI

The sensitivity and specificity of the UA were calculated for age subgroups. Exact prevalence of UTIs could not be calculated because not all patients had urine obtained for culture; however, a minimum estimate of prevalence or the "detected" prevalence was calculated for age and sex subgroups as the number of positive urine culture results per febrile child. A maximum estimate of prevalence was calculated as the number of UTIs diagnosed per number of cultures performed (by subgroup). The likelihood of a UTI with a negative UA result was calculated as a negative likelihood ratio ([1−sensitivity]/specificity). The posttest probability of a UTI after a negative UA result was estimated using the nomogram for Bayes' theorem[9] based on pretest probabilities (using detected prevalence) and the likelihood ratio.

Statistical analyses were conducted using the Statistical Program for the Social Sciences version 6.1.1 (SPSS, Chicago, Ill). Medians and interquartile ranges (IQRs) (25th-75th percentile) were provided for non-normal data. Mean values of interval data were compared between groups using a 2-tailed *t* test. EpiInfo Version 6.04b (Centers for Disease Control and Prevention, Atlanta, Ga) was employed for χ^2 and Fisher exact tests of nominal data. Confidence intervals for proportions were calculated using Stata Version 6 (Stata Corp, College Station, Tex). The institutional review board of the hospital approved the study.

tion) and therefore, knowing which patients may be adequately screened by a "bag" UA is of great importance to clinicians.

We undertook this study to measure the sensitivity of the standard UA for detecting UTI, to determine if sensitivity varies by age of the patient, and to offer recommendations for when a urine culture, and not just a screening UA, should be obtained.

RESULTS

STUDY GROUPS

Thirty-seven thousand four hundred fifty children younger than 2 years with temperature greater than or equal to 38°C were evaluated in the emergency department during the study period. Of these, 16523 children (44%) were girls and the median age and temperature were 10.6 months (IQR, 5.8-16.2 months) and 38.8°C (IQR, 38.3C°-39.5°C), respectively. Seventy-five percent (27942) had a designation of race recorded at registration in the emergency department. Thirty-four percent of these children were identified by their parents as white, 31% as black, 30% as Hispanic, 1.7% as Asian, and 3.3% as other. A UA was performed on 17679 patients (47%). Urine cultures were obtained from 11089 patients (30%); 53% were girls and the median age and temperature were 5.8 months (IQR, 2.0-12.2 months) and 39.0°C (IQR, 38.3°C-39.6°C), respectively. A paired UA and urine culture from each of 8815 patients was sent for evaluation. Seven hundred five culture results (8.0%) were positive and 115 cultures (1.3%) were contaminated. An additional 2274 urine cultures were sent without a paired UA; 80 of these culture results (3.6%) were positive and 29 (1.3%) were contaminated. Of the positive urine culture results (n=785), 86% were obtained by catheterization, 9% by suprapubic aspiration, and 5% by clean void. Of the positive culture results obtained by bladder catheterization, 88% yielded greater than 50000 cfu/mL. The common urine pathogens were *Escherichia coli* (82%), *Klebsiella* species (5%), enterococcus (3%), *Enterobacter* species (2%), and *Proteus* species (2%).

An audit of 250 medical records from our study group revealed concurrent antibiotic use in 14% (95% confidence interval [CI], 10%-19%) and previously diagnosed urologic abnormalities in 1.6% (95% CI, 0.4%-4.0%).

Table 1. Sensitivity of the Standard UA (Dipstick and Microscopy) for Identifying UTI by Age*

Age Group, mo	No. of Paired UA-UC	No. (%) of UTIs/Paired UA-UC	Sensitivity of Dipstick and Microscopy, % (95% CI)	Specificity of Dipstick and Microscopy, % (95% CI)
0-1	868	73/868 (8.4)	82 (71-90)	92 (90-94)
>1-3	2283	172/2283 (7.5)	82 (75-87)	94 (93-95)
>3-6	1349	162/1349 (12.0)	86 (79-91)	93 (91-94)
>6-9	1081	108/1081 (10.0)	82 (74-89)	92 (90-94)
>9-12	969	71/969 (7.3)	76 (64-85)	91 (89-93)
>12-18	1364	69/1364 (5.1)	80 (68-88)	91 (89-92)
>18-24	901	50/901 (5.5)	84 (70-93)	91 (89-93)
All Groups	**8815**	**705/8815** (8.0)	82 (79-84)	92 (91-92)

*UA indicates urinalysis; UTI, urinary tract infection; UC, urine culture; and CI, confidence interval.

Table 2. Detected Prevalence of UTIs in Febrile Children by Age and Sex*

Age Group, mo	Percentage of Febrile Patients With UC†	Prevalence, %‡	Prevalence, %‡	
			Females	Males
0-1	92 (1039/1123)	6.9 (7.5)	5.1 (6.8)	8.5 (10.7)
>1-3	80 (2729/3426)	5.5 (7.0)	5.9 (8.8)	5.3 (7.9)
>3-6	33 (1711/5126)	3.6 (10.9)	5.1 (15.7)	2.5 (11.4)
>6-9	24 (1403/5816)	2.1 (8.6)	3.7 (15.2)	0.8 (6.0)
>9-12	23 (1279/5601)	1.4 (6.2)	2.3 (7.2)	0.7 (5.4)
>12-18	19 (1767/9341)	0.8 (4.3)	1.4 (7.0)	0.4 (3.6)
>18-24	17 (1161/6984)	0.8 (4.7)	1.4 (7.3)	0.3 (3.8)
All Groups	30 **(11 089/37 450)**	2.1 (7.1)	2.9 (10.0)	1.5 (6.8)

*UTI indicates urinary tract infection; UC, urine culture.
†Data in parentheses are the proportion of febrile children who had a urine culture obtained.
‡Data in parentheses are estimates of maximum prevalence of urinary tract infections (number of UTIs per urine culture).

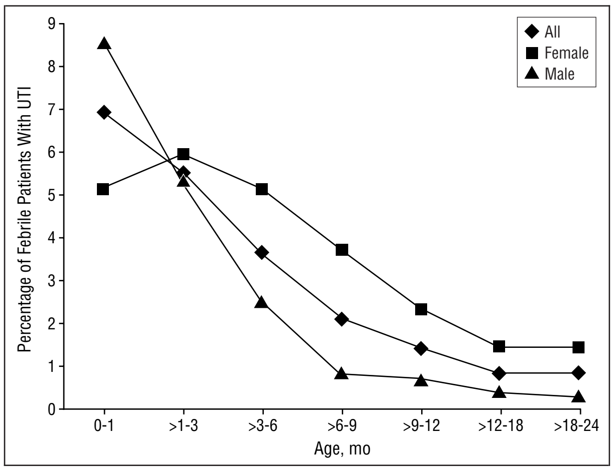

Figure 1. *The detected prevalence of UTI (urinary tract infection) by age and sex.*

URINALYSIS

Dipstick results were positive for LE and nitrite in 78% and 10% of those with culture-proven UTI, respectively. Pyuria was observed in 71% of those with UTI. The sensitivity and specificity of the UA by age is presented in **Table 1**. The overall sensitivity for dipstick analysis alone was 79% (95% CI, 76%-82%), and the sensitivity of combined dipstick and microscopy (standard UA performed in our laboratory) was 82% (95% CI, 79%-84%). The specificity of the UA (combined dipstick and microscopy) was 92% (95% CI, 91%-92%). The likelihood ratios for positive and negative UA results were 10.6 (95% CI, 10.0-11.2) and 0.19 (95% CI, 0.18-0.20). When only those catheterized specimens yielding greater than 50 000 cfu/mL were considered a UTI, 72 of the patients with UTI were recoded as not having a UTI and the sensitivity for the UA (dipstick and microscopy) increased to 85% (95% CI, 82%-88%) and the specificity decreased to 78% (95% CI, 77%-79%).

PREVALENCE OF UTI IN THE STUDY GROUP

The detected prevalence of UTIs among febrile patients (n=37 450) is presented in **Table 2** and **Figure 1**; maximum estimates of prevalence based on the number of urine cultures are also presented in Table 2. The prevalence of UTI by age, race, sex, and temperature is provided in **Table 3**. White girls had the highest prevalence of UTI, and among boys, Hispanic patients had the highest prevalence. The prevalence of UTI was also higher among children with temperatures greater than or equal to 39°C than among those with temperature 38°C to 38.9°C (P<.001).

The posttest probability of a UTI in the presence of a negative UA is presented in **Table 4**.

Figure 2 shows the use of study patients to determine the prevalence of UTI and the test characteristics of the UA.

COMMENT

Because the signs and symptoms of UTI are mostly nonspecific or absent in young children, the decision to investigate the urine as a possible source of fever must rely on the prior probability of UTI as determined by age, sex, race, temperature, and the potential for an alternative source of fever. Currently, there is no generally accepted strategy for screening febrile children for UTI. Most clinicians agree that very young, febrile infants require a proper urine culture (usually by bladder catheterization or suprapubic aspiration) for diagnosis,[10] and those patients with abnormal UA results require a urine culture. However, whether older febrile infants "require" a screening UA or a urine culture regardless of the UA result (especially if considering empiric antibiotic therapy)

Table 3. Detected Prevalence of UTIs Among Subgroups of Age, Sex, Temperature, and Race*

Group by Race and Temperature	Group by Age, mo: 0-6	>6-12	>12-18	>18-24	All
Girls					
White					
38-38.9°C	6.5 (12.2)	2.6 (12.0)	3.1 (16.0)	2.0 (13.1)	4.2 (12.7)
≥39°C	13.2 (20.2)	6.4 (12.5)	1.5 (4.6)	3.6 (11.5)	6.1 (15.0)
Black					
38-38.9°C	1.4 (3.8)	0.5 (5.8)	0.2 (2.6)	0	0.6 (3.3)
≥39°C	5.4 (11.4)	1.6 (5.6)	0.4 (1.8)	1.2 (4.9)	1.6 (5.8)
Hispanic					
38-38.9°C	1.7 (4.2)	2.1 (17.3)	0.2 (2.2)	0.3 (3.2)	1.3 (6.4)
≥39°C	5.7 (10.7)	3.7 (12.1)	2.5 (10.6)	1.4 (5.3)	3.1 (10.0)
All females†					
38-38.9°C	3.6 (7.9)	1.9 (12.2)	1.2 (8.8)	0.9 (8.1)	2.2 (8.8)
≥39°C	9.6 (16.4)	4.1 (12.8)	1.5 (6.1)	1.9 (7.0)	3.8 (11.4)
Boys					
White					
38-38.9°C	2.5 (5.0)	0.6 (6.5)	0.3 (2.7)	0	1.2 (4.7)
≥ 39°C	5.8 (10.4)	0.8 (3.6)	0.3 (2.0)	0.9 (6.9)	1.7 (6.8)
Black					
38-38.9°C	1.9 (6.1)	0	0.3 (4.1)	0.2 (5.9)	0.6 (5.2)
≥39°C	5.3 (12.1)	0.9 (4.9)	0	0	1.0 (5.5)
Hispanic					
38-38.9°C	4.4 (11.8)	0.9 (10.6)	0.5 (9.1)	0.3 (5.9)	1.8 (11.1)
≥ 39°C	11.8 (26.7)	1.4 (6.1)	0.8 (5.4)	0.7 (6.5)	2.5 (12.7)
All males†					
38-38.9°C	3.0 (7.3)	0.6 (2.6)	0.4 (5.9)	0.2 (3.1)	1.3 (7.0)
≥39°C	6.9 (14.0)	0.9 (5.0)	0.4 (2.5)	0.5 (4.1)	1.6 (7.9)

*Data are given as prevalence (percentage) with maximum prevalence in parentheses. UTI indicates urinary tract infection.

†Not all patients had a designation of race recorded and others were included in different race categories.

Table 4. Consequence of Using a UA Screen for UTI on Febrile Patients*

Pretest Probability (Prevalence), %	Posttest Probability of UTI With Negative UA, %	No. of Febrile Children Screened for Each Missed UTI
3.0	0.6	160
2.5	0.5	200
2.0	0.4	250
1.5	0.3	333
1.0	0.2	500
0.5	0.1	1000

*Two assumptions are made: (1) the likelihood ratio of a negative urinalysis (UA) findings is 0.19 and (2) urine is cultured only when the urinalysis finding are positive. UTI indicates urinary tract infection.

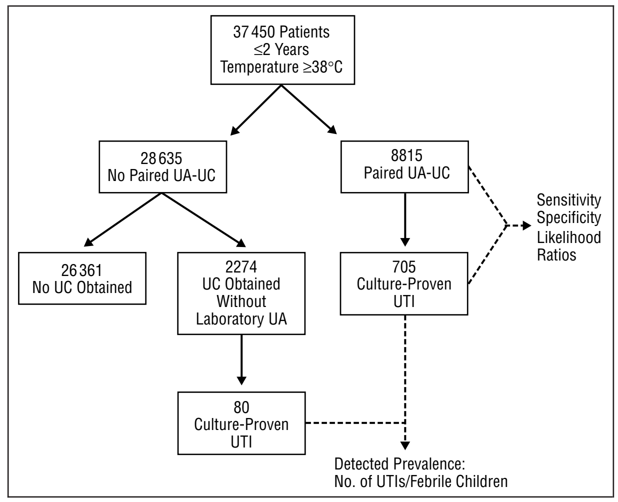

Figure 2. *Use of study patients for (1) determining test characteristics of urinalysis (UA) and (2) measuring prevalence. UC indicates urine culture; UTI, urinary tract infection.*

is controversial. This decision is magnified by the invasiveness of proper urine culture testing compared with noninvasive bag specimens that can be used for a screening UA. Three issues must be addressed first: (1) the prevalence of UTI, which varies by age, race, sex, and temperature; (2) the sensitivity of the standard UA for detecting UTI so clinicians can make decisions regarding treatment at the time of the patient's evaluation; and (3) the likelihood of missing a UTI if a clinician accepts a negative UA result as sufficient evidence that a culture is not needed.

The prevalence of UTI in children has been previously reported, but the study populations, definitions of UTI, and urine collection methods have varied.[1,7,11-14] In a large population-based study in Sweden, Marid and Jodal[15] found a cumulative incidence rate for symptomatic UTI to be 6.6% for girls and 1.8% for boys among children younger than 6 years. Hoberman et al[1] diagnosed UTI in 5.3% of 945 febrile infants younger than 1 year. The same authors also noted an overall prevalence of 7.5% among those without another potential source of fever and 17% for white girls with temperature higher than 39°C. In the largest prospective prevalence study of UTI among febrile children, Shaw et al[2] collected catheterized urine specimens for culture from febrile (temperature ≥38.5°C) boys younger than 1 year and girls younger than 2 years who did not have another definite source of fever by examination (bronchiolitis, stomatitis, cellulitis, perforated otitis media, croup, or varicella) or were not concurrently taking antibiotics. In their study of 2908 children, 83% of eligible patients had a urine culture obtained; the prevalence of UTI was 3.3% (80/2411; 95% CI, 2.6%-4.0%), including 5.9% of children without an alternative potential source of fever and 16% of white girls. In our study, the detected prevalence for febrile children younger than 2 years was 2.1% (785/37 450) (95% CI, 2.0%-2.1%) overall and 2.9% and 1.5% for girls and boys, respectively. Boys accounted for most UTIs in the first 2 to 3 months, and then girls predominated in agreement with earlier reports.[2,7,13,16-19] Higher fever (temperature ≥39°C) compared with lower fever (temperature 38.0°C-38.9°C) was associated with higher prevalence, especially during the first year of life. By sex and race, the prevalence of UTI for girls was 5.0% in white patients, 2.1% in Hispanic patients, and 1.0% in black patients. Among boys, the rate was 2.2% in Hispanic patients, 1.4% in white patients, and 0.8% in black patients. The higher rate of UTIs among Hispanic boys has not been previously reported; however, the significance could not be properly evaluated because circumcision status varies by race. When patients were divided into subgroups based on age, race, sex, and temperature, prevalence varied between 0% (black boys >12 months) and 13% (white girls <6 months with temperature ≥39°C).

Previous investigators have reported on the sensitivity of the various components of the UA to detect UTI, including dipstick LE and nitrite, microscopy for WBCs and bacteria, and Gram stains.[14,20-26] Differences in the study populations make it difficult to compare and interpret the results of these studies. Lohr[21] found the sensitivity of the UA (dipstick and microscopy) to be 88% in children grouped together from 1 month to 16 years of age. Hoberman[24] found a sensitivity of 54% for pyuria (≥5 WBC per high-power field) in febrile infants younger than 1 year. Shaw et al[14] reported the sensitivity of dipstick plus microscopy to be 83% in febrile boys younger than 6 months and girls younger than 2 years. Among children younger than 8 weeks, Crain and Gershel[7] found the sensitivity of the UA (pyuria and bacteriuria) to be 48%. Our study was the first to evaluate whether the sensitivity of the UA varied with age. We found the sensitivity of UA to be 82% and constant for age subgroups among febrile children younger than 2 years. The sensitivity did improve with higher concentrations of bacteria in accordance with the findings of others.[22,23,27]

The dipstick analysis (± microscopy) is the most common form of UA, and has recently been evaluated as the most cost-effective screen for UTI in young infants.[14] An "enhanced urinalysis" as proposed by Hoberman et al[28] is composed of hemocytometer-determined pyuria (≥10 WBCs/mm^3) and an unspun Gram stain for bacteriuria with a reported sensitivity of 96%[14]; however, for practical reasons this technique has yet to be adopted in most clinical laboratories or office practices. Likewise, Gram stains of unspun urine have been reported to be very sensitive (94%) for UTI, but are impractical for office-based settings.[20,29]

The probability of a missed UTI because of a false-negative UA result can be estimated using the likelihood ratio of a negative test result and the prevalence of UTIs. Our data demonstrate that the sensitivity and specificity, and thus the likelihood ratio for a negative test result, do not vary by age. However, because the prevalence of UTI is high in young infants, the absolute number of false-negative results is also high; so despite a constant sensitivity for UTI, the UA does not perform as well in younger infants. As demonstrated, the prevalence of UTI varies with age, sex, temperature, and race, which can be used to estimate the risk of missing a UTI. An acceptable risk is not a mathematical or statistical function, but a clinician-dependent function. Clinicians should consider the likelihood of UTI in a particular patient based on all of the clinical variables and then decide whether the patient needs to be tested for a UTI. The clinician must then decide whether a negative UA result is sufficient or whether the risk of missing a UTI is still significant enough to warrant obtaining a urine culture. We suggest that in the absence of empiric antibiotic therapy, if the prevalence of UTI is less than 2% in a given population, the risk of missing a UTI because of a false-negative UA result is "acceptable." A prevalence of 2% would predict that 1 UTI would be missed (false-negative UA result) for every 250 febrile infants screened by UA. Based on our minimum estimates of prevalence, urine cultures should therefore be obtained in all boys younger than 6 months and girls younger than 12 months without an alternative source of fever. This strategy (using a 2% prevalence) based on age and sex can be further refined with variables such as temperature and race; for example, white girls with a temperature greater than 39°C still have a UTI prevalence of 3.6% at age 24 months, which would still warrant a urine culture regardless of the UA result. Because our detected prevalence represents minimum estimates of true prevalence, the data can be used confidently to determine who needs urine testing, but it should be used conservatively to exclude patients from testing. From a practical standpoint, the risk of missing a UTI in practice is much higher when a patient is not considered to be at risk for a UTI (ie, no UA is done) than because of a false-negative UA result.

Several limitations are inherent to the study. Most importantly, the retrospective design does not allow interpretation of why patients had or did not have a UA or urine culture obtained. Forty-seven percent of all febrile patients had a UA and 30% had a urine culture; this is comparable to the 2 previous prospective studies of prevalence in which 38% (Hoberman et al[1]) and 54% (Shaw et al[2]) of febrile infants had cultures performed. Accordingly, the detected prevalence of UTI represents a minimum estimate of true prevalence of UTI because (1) not all patients had urine cultures and (2) we used all febrile patients as the denominator in this calculation, regardless of whether a urine culture was obtained or whether the patient had an alternative source of infection. Additionally, the concurrent use of antibiotics, as estimated in the audit of patient records, biases the data toward minimum estimates of prevalence and falsely decreases our estimates of the specificity of the UA for UTI.

In conclusion, the prevalence of UTI among febrile children varies with age, sex, race, and temperature. An incremental increase in risk for UTI is associated with younger age, being white and female, and higher fevers. The sensitivity of the standard UA is 82% and does not vary by age for children younger than 2 years. A negative UA result decreases the odds of a UTI 5-fold (likelihood ratio, 0.19). In combination with the prevalence of UTI, the risk of missing a UTI based on a false-negative UA result can also be calculated. Clinicians can therefore use the patient-specific estimates of risk for a UTI to determine when the UA is an adequate screening test and which patients will require a urine culture regardless of the UA result.

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