Urinalysis Predictive of Urine Culture Results

Boyd L. Bailey, Jr, MD
Selma, Alabama

Background. Most clinicians treat patients for presumptive urinary tract infections based on urinalysis findings. Which of these findings is the best predictor of infection?

Methods. A retrospective cross-sectional study of 202 serial subjects of all ages was conducted over 8 months in a typical family medicine setting. Urinalysis and culture were performed concurrently.

Results. The best predictors for significant bacteriuria (defined as a culture with more than 50,000 colony-forming units) were ≥2+ bacteriuria (sensitivity, 0.74; specificity, 0.80), or ≥10 white blood cells per high-power field (sensitivity, 0.816; specificity, 0.651), or a positive nitrite test (sensitivity, 0.395; specificity, 0.929). The optimal combination of any two of the three predictor variables also was determined.

Conclusions. Standard urinalysis results can be highly predictive of infection in typical family practice patients.

Key words. Urinary tract infections; sensitivity and specificity; data interpretation, statistical.
(J Fam Pract 1995; 40:45-50)

The predictability of a urinary tract infection from semiquantitative measures of the urinalysis, such as bacteriuria and pyuria, is well documented in the review literature.[1-3] The use of the rapid screening estimates for bacteriuria and pyuria is presented in a number of studies,[4-8] but the nature of these semiquantitative estimates can lead to uncertainty in the predictive value of these measures, either individually or in combination with the nitrite test. This study is an attempt to establish whether the screening methods used in one family medicine clinic are useful in predicting significant bacteriuria. The results are presented using current mathematical concepts not ordinarily used in combination in previous reports on this subject in the literature. These concepts encompass ROC (receiver operating characteristic) curve analysis, sensitivity, specificity, and positive and negative likelihood ratios, with 95% confidence intervals (CI) presented when appropriate. This approach, especially with regard to 95% confidence intervals,[9] makes for a clearer presentation and understanding of the limitations of the calculated results.

A number of reviews have compiled individual reports on predictors of focused interest here: bacteriuria, pyuria, and nitrite status. Of note are reviews by Lohr,[2] Hollander et al,[7] and Jenkins et al.[3] In the review by Jenkins et al of published studies of uncentrifuged, unstained urine microscopy for bacteriuria, sensitivity for various presumed optimal cutoffs (actual figures rather than 95% CI range) ranged from 0.66 to 0.97, and specificity from 0.50 to 1.00. In the pediatric review by Lohr, nitrite sensitivity ranged from 0.21 to 0.727, and specificity from 0.949 to 0.996. In the adult study by Hollander et al, nitrite sensitivity was 0.63 and specificity 0.98. In Lohr's review, the optimum pyuria cutoff (approximately ≥5 white blood cells per high-power field [hpf]) showed sensitivities ranging from 0.548 to 0.81).

With some inherent flaws, the urine culture remains the reference standard for confirming the existence of significant bacteriuria and urinary tract infection. Literature reports[10,11] for positive cultures range from a low of 100 colony-forming units per milliliter (CFU/mL) to the higher and widely published 100,000 CFU/mL. Confirmation of the best diagnostic level of significant bacteriuria, as measured by a culture, is beyond the scope of this study. Therefore, an optimum diagnostic cutoff for bacteriuria has been chosen arbitrarily; against this optimum cutoff, we have intentionally forced the decision threshold to vary, and thus constructed a ROC curve. The physician

Submitted, revised, August 4, 1994.

From the University of Alabama at Birmingham/Selma Family Medicine Residency Program in Selma. Requests for reprints should be addressed to Boyd L. Bailey, MD, UAB/Selma Family Medicine Center, 429 Lauderdale St, Selma, AL 36701.

ISSN 0094-3509

gains the most from a test when the pretest probability (prevalence or prior probability) of the disorder is .50 (the "50:50" dilemma), or more leniently, .40 to .60.[12]

With a tendency to maintain the urinalysis as an inexpensive, practical, and quick test, the measures in question generally become approximations of known quantitative methods, and thus are semiquantitative. This applies especially to the concentration of white blood cells and bacteria in the urine. In terms of WBC/hpf, a study by Alwall[13] has documented very good correlation between strict quantitative counting chamber methods and quick semiquantitative estimates of spun samples under a cover slip on a slide. The utility of these widely used semiquantitative estimates will be explored here.

Methods

The study was performed at the Selma Family Medicine Center, an affiliate of the University of Alabama at Birmingham. The data were collected retrospectively by studying serial encounters of 202 unselected urine samples that included both urinalysis and urine cultures on patients seen between February 1992 and November 1992. The samples were taken from subjects for the following reasons: they had either symptoms or signs of a urinary tract infection (UTI); the physician had reason to suspect an infection; or the physician wanted to demonstrate resolution of a recent infection.

Of the 202 cases, 166 were nonpregnant female patients ranging in age from 3 to 98 years (mean, 49.3 years). Thirty-six were male patients ranging in age from 9 months to 102 years (mean, 50.2 years). The culture outcome, in terms of diagnostic level of pathogenic colony count established arbitrarily at 50,000 CFU/mL, was compared with three common urine screening indicators: pyuria (WBC/hpf), bacteriuria, and positive nitrite test. This group was then analyzed with regard to the predictability of these rapid screening methods for significant bacteriuria as measured by a positive culture.

Diagnostic criteria. Considering that colony counts of less than 100,000 per milliliter are often considered clinically significant, the author decided that the cutoff should be less than 100,000; 50,000 CFU/mL was arbitrarily chosen as the cutoff for significant bacteriuria.

Laboratory testing. Testing had been carried out by regular laboratory personnel at our clinic in the accustomed practice of day-to-day operation. The urine specimens had been transported to a commercial laboratory according to specified guidelines for ordinary clinic function. A retrospective study such as this does not allow correction for inherent flaws, most notably urine culture inaccuracies that might occur as a result of transport. Personnel were polled as to the technique of wet-slide preparation and the method of estimating WBC and bacteria concentration. There was agreement among the personnel that consistent estimating techniques were used during the study period. Interrater reliability was not measured in this study, and should be considered a limitation. No staff member, including laboratory personnel, was informed of this study before its start. Because the study was retrospective, there was no opportunity to standardize techniques beyond what was required for daily laboratory operation.

Reference method. Clean-catch specimens had been collected and placed in Vacutainer (Becton-Dickinson, Rutherford, NJ) urine transport kits within 60 minutes of collection. These kits were labeled and stored according to manufacturer's instructions at room temperature until picked up by the outside reference laboratory, which usually occurred within 8 hours of collection. Depending on the time of day, the specimen may have remained in the transport medium for as long as 15 hours. The inoculation of the specimen to a culture medium at the reference laboratory could generally be expected to be performed within 4 hours of the pickup.

The specimen workup procedure involved stratifying colony counts in three sets: $<10{,}000$ CFU/mL, $\geq 10{,}000$ but $<100{,}000$ CFU/mL, and $>100{,}000$ CFU/mL. For colony counts of $>10{,}000$ CFU/mL, two or more organisms could be considered significant.

In this study, *Escherichia coli* or other gram-negative rods, enterococci, *Staphylococcus saprophyticus* (in young women), and group B streptococci were considered as common pathogens. *Campylobacter, Haemophilus influenzae* (usually in children), *Gardnerella* (usually in pregnant women), *Corynebacterium* group JK c, *Corynebacterium* D2, *Ureaplasma,* and *Streptococcus pneumoniae* were considered as uncommon.

Sediment analysis. Ten milliliters of freshly voided urine (less than 2 hours old) had been placed in a centrifuge tube and spun for 3 to 5 minutes. The supernatant was poured off, leaving approximately 0.25 to 0.50 mL of specimen and sediment. One drop of this was placed under ×400 microscopic examination.

The number of WBC/hpf was estimated, based on an actual count of up to approximately 30 WBC/hpf. Beyond that, the number of WBC/hpf was estimated up to 80 (too numerous to count). Three fields were examined in this manner and the results averaged.

On the same slide, under ×400 magnification, bacteria were estimated using a variation reported in the literature[3,8] and assigned a score ranging from trace through 4+. Each step of this process is defined in Table 1.

Nitrite test. The chemical principle for the nitrite test

Table 1. Estimation of Bacteria on Screening Urinalysis

Bacteria Score Assigned	Descriptive Findings on Slide
Trace	Few bacteria scattered about
1+	No problem seeing other sediment
2+	Many bacteria, covering about half the slide, but not enough to cause loss of formed element definition
3+	The bacteria are prevalent enough to partially cause loss of the formed element definition
4+	All formed elements have significant loss of definition by the bacteria

is stated in the reagent strip package insert: "This test depends on the conversion of nitrate (derived from the diet) to nitrite by the action of Gram negative bacteria in the urine. At the acid pH of the reagent area, nitrite in the urine reacts with ρ-arsanilic acid to form a diazonium compound. This diazonium compound in turn couples with 1,2,3,4-tetrahydrobenzo(h)quinoline-3-01 to produce a pink color."[14]

Calculations and Statistics

Confidence intervals for sensitivity and specificity were calculated in the standard manner for single sample proportions.[9] The confidence intervals for likelihood ratio were calculated by an adaptation of the method for odds ratio as outlined by Morris and Gardner.[15]

Results

The summary of screening data translated into true negatives, false positives, true negatives, and false negatives based on 50,000 CFU/mL as the diagnostic level for true UTI is presented in Table 2. These data formed the basis for intentionally forcing the decision threshold to vary. From this set of thresholds, which is summarized in Table 3, ROC curves for pyuria, bacteriuria, and combinations were constructed (Figures 1, 2, and 3). Standard principles of ROC construction and analysis were followed.[16]

Figure 1 is the ROC curve for pyuria. Following the general principle that the optimum decision threshold is the point on the curve closest to maximum true positive rate (or closest to 1.0), one has to empirically choose among the three points (10, 15, or 22 WBC/hpf). In view of the relative noncritical nature of urine testing, the author chose 10 WBC/hpf as the optimum point of the threshold.

With regard to bacteriuria, as shown in Figure 2, a more straightforward curve is produced with less ambiguity found in the threshold of the index of 2+. The choice could be shifted to the more lax index value of 1+, but in the author's opinion, this value would be too lax.

An overlay of the ROC curves for the different colony counts of 10,000 CFU/mL and 100,000 CFU/mL that could possibly define the diagnostic level of significant bacteriuria is shown. This overlay illustrates that similar conclusions can be drawn at colony counts ranging from 10,000 CFU/mL to 100,000 CFU/mL.

Table 2. Summary of Screening Data at Diagnostic Level of 50,000 CFU/mL

Predictors of Positive Cultures	True Negatives	False Positives	True Positives	False Negatives
Bacteriuria				
1+	58	68	68	8
2+	101	25	56	20
3+	118	8	33	43
4+	123	3	18	58
Pyuria (WBC/hpf)				
5	60	66	69	7
10	82	44	62	14
15	90	36	53	23
22	103	23	45	31
42	109	17	37	39
Nitrite	103	9	30	46
Combinations of above 3 predictors				
Bacteria=2+, WBCs=10, Nitrite+				
Any 1	68	58	72	4
Any 2	109	17	54	22
Bacteria=2+, WBCs=15, Nitrite+				
Any 1	74	52	70	6
Any 2	111	15	48	28

CFU denotes colony-forming unit; WBC, white blood cell; hpf, high-power field.

Table 3. Summary of the Calculated Sensitivities, Specificities, Likelihood Ratios, Positive and Negative Predictive Values, with Pertinent 95% Confidence Intervals at the Diagnostic Level of 50,000 CFU/mL

Predictors of Positive Cultures	Sensitivity	Sensitivity 95% Confidence Interval	Specificity	Specificity 95% Confidence Interval	Positive Likelihood Ratio (LR)	Positive LR Confidence Interval	Negative Likelihood Ratio	Negative LR Confidence Interval
Bacteriuria								
1+	0.895	0.826 to 0.964	0.46	0.373 to 0.547	1.658	1.387 to 1.982	0.229	0.116 to 0.452
2+	**0.737**	**0.638 to 0.836**	**0.802**	**0.732 to 0.871**	**3.714**	**2.550 to 5.408**	**.328**	**0.223 to .483**
3+	0.434	0.323 to 0.546	0.937	0.894 to 0.979	6.839	3.335 to 14.022	0.604	0.494 to 0.739
4+	0.237	0.141 to 0.332	0.976	0.950 to 1.003	9.947	3.030 to 32.654	0.782	0.688 to 0.889
Pyuria (WBC/hpf)								
5	0.908	0.843 to 0.973	0.476	0.389 to 0.563	1.733	1.446 to 2.078	0.193	0.093 to 0.401
10	**0.816**	**0.729 to 0.903**	**0.651**	**0.568 to 0.734**	**2.336**	**1.799 to 3.033**	**.283**	**0.173 to .462**
15	0.697	0.594 to 0.801	0.714	0.635 to 0.793	2.441	1.784 to 3.339	0.424	0.296 to 0.606
22	0.592	0.482 to 0.703	0.817	0.750 to 0.885	3.244	2.144 to 4.907	0.499	0.376 to 0.662
42	0.487	0.374 to 0.599	0.865	0.805 to 0.925	3.608	2.191 to 5.942	0.593	0.472 to 0.746
Nitrite	**0.395**	**0.285 to 0.505**	**0.929**	**0.881 to 0.976**	**5.526**	**2.784 to 10.97**	**.652**	**0.539 to .788**
Combinations of above 3 predictors								
Bacteria = 2+, WBC = 10, Nitrite +								
Any 1	0.947	0.897 to 0.998	0.54	0.453 to 0.627	2.058	1.691 to 2.505	0.098	0.037 to 0.257
Any 2	**0.711**	**0.609 to 0.812**	**0.865**	**0.805 to 0.925**	**5.266**	**3.308 to 8.383**	**.335**	**0.234 to .479**
Bacteria = 2+, WBC = 15, Nitrite +								
Any 1	0.921	0.860 to 0.982	0.587	0.501 to 0.673	2.232	1.794 to 2.777	0.134	0.062 to 0.294
Any 2	0.632	0.523 to 0.740	0.881	0.824 to 0.937	5.305	3.202 to 8.791	0.418	0.309 to 0.565

NOTE: The highlighted rows in each section represent the optimum decision thresholds as determined by the ROC curves in Figures 1 through 3, and the single set of nitrite data.
CFU denotes colony-forming unit; WBC, white blood cell; hpf, high-power field.

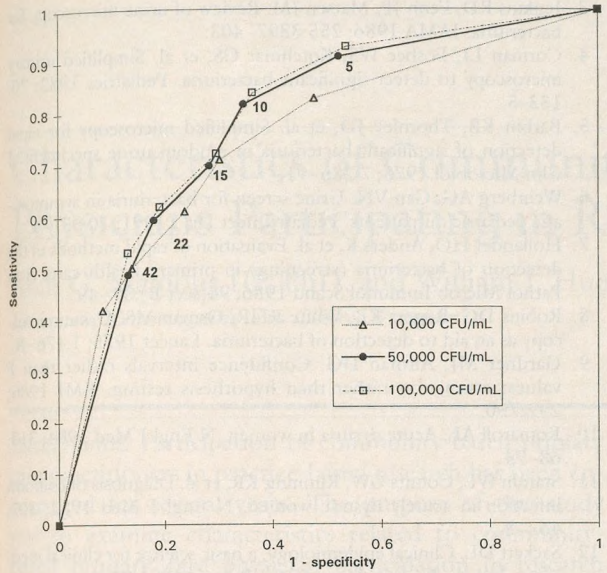

Figure 1. The ROC curve for estimating the best level of pyuria based on a "positive" culture of 50,000 colony-forming units per milliliter (CFU/mL). Other cutoffs of 10,000 and 100,000 CFU/mL are shown to illustrate the effect on the decision thresholds should these values be chosen.

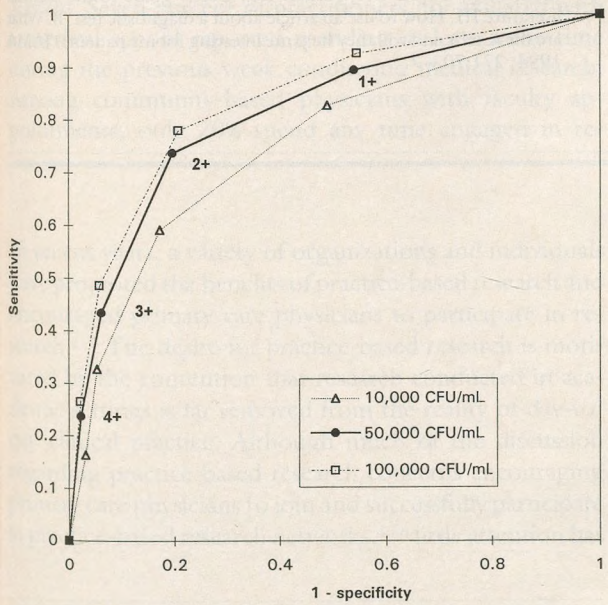

Figure 2. The ROC curve for estimating the best level of bacteriuria based on a "positive" culture of 50,000 colony-forming units per milliliter (CFU/mL). Other cutoffs of 10,000 and 100,000 CFU/mL illustrate the effect on the decision thresholds should these values be chosen.

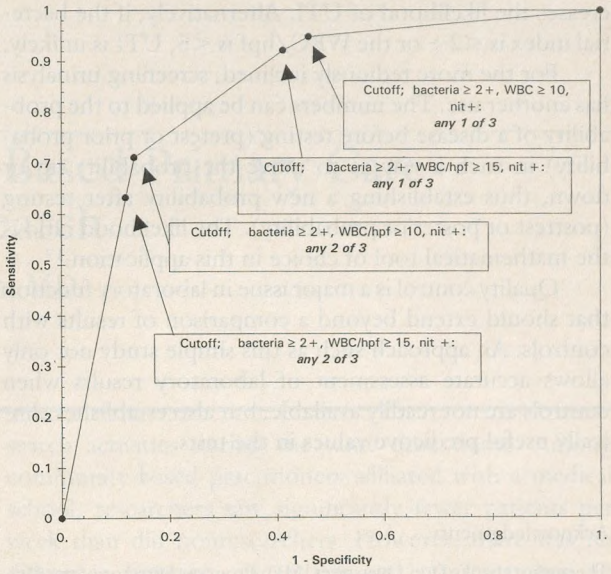

Figure 3. The ROC curve for estimating best level of combinations of bacteriuria, nitrite, and pyuria based on a "positive" culture of 50,000 colony-forming units per milliliter (CFU/mL).

Combinations of three indicators, as presented in Figure 3, fall on a stepwise discrimination continuum, again presenting a choice among two or more points on the curve. The point defined by any two of bacteria >2+, WBC/hpf >15, and nitrite positive is probably best, even though a bit strict. The next point on the curve up and to the right is judged by the author to be too lax. For clarity, this figure does not show an overlay of different colony counts.

Discussion

There are obviously a few patients with urinalysis findings that are highly predictive of infection. A woman with dysuria, pyruia, bacteriuria, and a positive nitrite test has a high likelihood of infection. What is the clinician to do when the combination of information is less suggestive or even contradictory (eg, pyruia without bacteriuria)? General conclusions about the value of each test for ruling in or ruling out a disease can be drawn from the specificity or sensitivity results in each category. That is, if a screening urinalysis shows either >2+ bacteriuria or >10 WBC/hpf or nitrite positive, there should be a relatively high suspicion for UTI. For example, if the bacterial index is 4+, UTI should be highly suspected. A combination of any two of the three indicators at the level of >2+ bacteria, >10 WBC/hpf, and nitrite positive further in-

creases the likelihood of UTI. Alternatively, if the bacterial index is <2+ or the WBC/hpf is <5, UTI is unikely.

For the more tediously inclined, screening urinalysis has another use. The numbers can be applied to the probability of a disease before testing (pretest or prior probability) in such a way as to move the probability up or down, thus establishing a new probability after testing (posttest or posterior probability). The likelihood ratio is the mathematical tool of choice in this application.[17]

Quality control is a major issue in laboratory function that should extend beyond a comparison of results with controls. An approach such as this simple study not only allows accurate assessment of laboratory results when controls are not readily available, but also establishes clinically useful predictive values in the tests.

Acknowledgments

The author thanks Don Overstreet, MD, Program Director of the University of Alabama/Selma Family Medicine Program, for his support; Michael Hardin, PhD, of the University of Alabama at Birmingham, School of Public Health, Department of Biostatistics, for statistical consultation; and Robert R. Speed, PhD, of the Alabama Reference Laboratory in Montgomery for providing information on microbiology.

References

1. Sheets C, Lyman JL. Urinalysis. Use of clinical laboratory in emergency medicine. Emerg Med Clin North Am 1986; 4:263–80.
2. Lohr JA. Use of routine urinalysis in making a presumptive diagnosis of urinary tract infection in children. Pediatr Infect Dis J 1991; 10:646–50.
3. Jenkins RD, Fenn JP, Matsen JM. Review of urine microscopy fo bacteriuria. JAMA 1986; 255:3397–403.
4. Corman LI, Foshee WS, Kotchmar GS, et al. Simplified urinar microscopy to detect significant bacteriuria. Pediatrics 1982; 70 133–5.
5. Barbin KB, Thornley JD, et al. Simplified microscopy for rapi detection of significant bacteriuria in random urine specimens. Clin Microbiol 1978; 7:286–91.
6. Weinberg AG, Gan VN. Urine screen for bacteriuria in symptom atic pediatric outpatients. Pediatr Infect Dis J 1991; 10:651–4.
7. Hollander HO, Anders K, et al. Evaluation of rapid methods of th detection of bacteriuria (screening) in primary health care. Acta Pathol Microb Immunol Scand 1986; 94(sect B):39–49.
8. Robins DG, Rogers KB, White RHR, Osman MS. Urine micros copy as an aid to detection of bacteriuria. Lancet 1975; 1:476–8
9. Gardner MJ, Altman DG. Confidence intervals rather than values: estimation rather than hypothesis testing. BMJ 198 292:750.
10. Komaroff AL. Acute dysuria in women. N Engl J Med 1984; 31 68–74.
11. Stamm WE, Counts GW, Running KR, et al. Diagnosis of colifor infection in acutely dysuric women. N Engl J Med 1982; 30 463–8.
12. Sackett DL. Clinical epidemiology, a basic science for clinical me icine. 2nd ed. Boston, Mass: Little, Brown, 1991:91–3.
13. Alwall N. Pyuria: deposit in high-power microscopic field—WBC hpf—versus WBC/mm^3 in counting chambers. Reappraisal of valuable clinical routine method (urinary sediment). Acta Me Scand 1973; 194:537–40.
14. Miles Inc, Diagnostic Division. Ames Reagent Strips . Elkhart, In Miles Inc, 1992.
15. Morris JA, Gardner MJ. Calculating confidence intervals for relati risks (odds ratios) and standardized ratios and rates. BMJ 198 296:1313–6.
16. Metz CE. Basic principles of ROC analysis. Semin Nucl Med 197 8(4):283–98.
17. Jaeschke R, Guyatt GH, Sackett DL. Users' guide to the medic literature III. How to use an article about a diagnostic test. B. Wh are the results and will they help me in caring for my patients? JAM 1994; 271:703–7.