Poor Predictive Ability of Urinalysis and Microscopic Examination to Detect Urinary Tract Infection

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Abstract

Results of urinalysis, particularly the leukocyte esterase and nitrite tests, often are used to determine whether treatment is needed or a culture will be performed in cases of suspected urinary tract infection. However, there is disagreement over the quality of urinalysis as a screening test for urinary tract infections. Final urine culture results (n = 225) were obtained from the clinical microbiology laboratory. Stepwise binary logistic regression was used to derive a model using presence of infection as determined by culture as the dependent variable and urinalysis results as independent variables. A second set of data (n = 128) then was obtained to test the model. Statistical significance and the ability to predict infection based on urinalysis results were determined. Results indicated a lack of sensitivity for leukocyte esterase, nitrite, and presence of bacteria in the microscopic examination as indicators of urinary tract infection.

Results of urinalysis, particularly the leukocyte esterase and nitrite tests, often are used to determine whether treatment is needed or a culture will be performed in cases of suspected urinary tract infection. Many clinicians interpret positive results in these tests as indicators of probable infection and use the results to guide patient treatment. However, there is disagreement about the quality of urinalysis as a screening test for urinary tract infections.

Previous studies have shown a correlation between positive leukocyte esterase and nitrite results and positive culture results. Lohr et al1 found that a combination of leukocyte esterase, nitrite, and microscopic examination for bacteria had a sensitivity of 100% for detecting urinary tract infection. They also showed the nitrite test to be 100% specific. Other studies have shown a lack of sensitivity and specificity for these tests for predicting a positive urine culture result. Lenke et al2 demonstrated a specificity of 100% for the nitrite test, but the sensitivity of nitrite was only 22%, greatly limiting its diagnostic value. Zaman and colleagues3 also found low sensitivities for leukocyte esterase, nitrite, and presence of bacteria.

Microscopy results have been found of questionable value for screening as well. Bailey4 determined that microscopic detection of moderate numbers of bacteria and leukocytes in the urine had sensitivities of less than 75% and 85%, respectively. The specificity for a combination of both tests was less than 85%. The positive predictive value of microscopic examinations for pyuria, bacteriuria, or both has been shown to be as low as 33%.1 Both of these studies1,4 used culture as the “gold standard.”

The purpose of the present study was to develop a statistical model for predicting urine culture results based solely on findings of urinalysis and microscopic examination. The
model then was tested to determine its clinical reliability. The effects of patient sex and age on the predictive ability of urinalysis results also were studied.

Materials and Methods

Two samples of urine specimens were obtained. Group 1 consisted of 225 voided urine specimens submitted to the clinical microbiology laboratory at the Medical University Hospital, Charleston, SC, for both urinalysis and urine culture. Automated urinalysis and microscopic examination were performed on all specimens using the Yellow Iris (IRIS, Chatsworth, CA) and Chemstrip (Boehringer Mannheim, Indianapolis, IN) urinalysis strips. The variables measured by urinalysis were pH, protein, glucose, bilirubin, nitrite, specific gravity, blood, ketones, urobilinogen, and leukocyte esterase. Microscopic elements evaluated were RBCs, WBCs, casts, epithelial cells, crystals, bacteria, yeast, and WBC clumps. The presence of infection was determined by quantitative culture on trypticase soy agar plus 5% sheep blood and MacConkey agar. Infection was defined as a total colony count of more than $10^4$ colony-forming units per milliliter, with the predominant organism being a recognized urinary tract pathogen. Specimens that yielded growth of multiple isolates with no predominating organism or heavy growth of normal urogenital flora (e.g., Lactobacillus species, Corynebacterium species) were considered contaminated.

Group 2, consisting of 128 urine specimens meeting the same criteria, was used to test the statistical model developed.

Statistical analysis was done using Minitab version 12 (Minitab, State College, PA). Binary logistic regression using the logit function was performed on group 1 to derive a model using presence of infection as determined by culture as the dependent variable and urinalysis and microscopic examination results as independent variables. A reverse stepwise approach was taken. All urinalysis and microscopic examination results were included in the initial regression model. After each analysis, the least significant variable was removed and the analysis repeated until all remaining variables were statistically significant ($P < .05$). Separate models also were created in the same manner using specimens in group 1 from male, female, geriatric, and pediatric patients.

Data from group 2 were used to test the model for ability to predict infection as determined by urine culture results. Sensitivity, specificity, and positive and negative predictive values were determined for the patient population as a whole and for male, female, geriatric, and pediatric subpopulations.

Results

Table 1 shows the culture results. In group 1, 33 (14.7%) of 225 cultures were positive for infection, while in group 2, 27 (21.1%) of 128 cultures were positive. In each sample, 66.7% of the positive cultures were gram-negative rods.

When each of the independent variables was tested individually for relationship with clinically significant culture results using binary logistic regression, the following variables were shown to be statistically significant: leukocyte esterase, presence of WBCs, presence of at least moderate numbers of bacteria, and nitrite. Leukocyte esterase and the presence of at least moderate numbers of bacteria demonstrated the strongest relationship with infection ($P < .001$ for both; odds ratios of 12.41 and 14.84, respectively). Blood, which has been shown to be related significantly to infection in another study, was not significant in this data set ($P = .218$).

By using reverse stepwise logistic regression analysis, all variables were eliminated as not statistically significant except leukocyte esterase and the presence of at least moderate numbers of bacteria. Therefore, the final model created used a combination of positive leukocyte esterase and the presence of at least moderate numbers of bacteria to predict infection. The $P$ values were less than .001 for both of these variables. While a positive nitrite result and presence of WBCs were significant when tested alone, they were not significant when controlling for leukocyte esterase and the presence of bacteria.

Separate models also were created in the same manner for specimens from male and female patients. In both cases, the final models included only the same 2 variables present in the model for all patients (data not shown). In the male model, leukocyte esterase had a $P$ value of .004 and an odds...
Table 2
Results of Univariate Logistic Regression on Each Variable

<table>
<thead>
<tr>
<th>Variable Tested</th>
<th>P</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reagent strip</td>
<td>.427</td>
<td>0.00</td>
</tr>
<tr>
<td>Specific gravity</td>
<td>.274</td>
<td>0.79</td>
</tr>
<tr>
<td>pH</td>
<td>.504</td>
<td>1.29</td>
</tr>
<tr>
<td>Glucose</td>
<td>.438</td>
<td>0.55</td>
</tr>
<tr>
<td>Protein</td>
<td>.569</td>
<td>1.29</td>
</tr>
<tr>
<td>Ketones</td>
<td>.892</td>
<td>1.16</td>
</tr>
<tr>
<td>Blood</td>
<td>.218</td>
<td>1.59</td>
</tr>
<tr>
<td>Nitrite</td>
<td>.019</td>
<td>5.13</td>
</tr>
<tr>
<td>Urobilinogen</td>
<td>.988</td>
<td>1.00</td>
</tr>
<tr>
<td>Leukocyte esterase</td>
<td>&lt;.001</td>
<td>12.41</td>
</tr>
<tr>
<td>Microscopic examination</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence of RBCs</td>
<td>.266</td>
<td>1.00</td>
</tr>
<tr>
<td>Presence of WBCs</td>
<td>.017</td>
<td>3.11</td>
</tr>
<tr>
<td>Squamous epithelial cells</td>
<td>.520</td>
<td>1.01</td>
</tr>
<tr>
<td>At least moderate numbers of bacteria</td>
<td>&lt;.001</td>
<td>14.84</td>
</tr>
<tr>
<td>Crystals</td>
<td>.356</td>
<td>1.69</td>
</tr>
</tbody>
</table>

Discussion

The present study was based on laboratory findings on a patient population consisting of tertiary care patients, ambulatory clinic, and family medicine patients. Of all the specimens tested, 17.0% were considered indicative of infection according to the hospital’s culture protocol. Of the positive cultures, 67% of the pathogens isolated were gram-negative bacilli, 25% were gram-positive cocci, and 8% were yeast.

It seems that while urinalysis and urine microscopic examination often are used to collect evidence for or against a urinary tract infection, none of the components of these tests should be relied on to make that diagnosis. Although the model of a positive leukocyte esterase test result and the presence of at least a moderate number of bacteria was statistically very strong, the negative predictive value of this model in all patients was still only 86.2%, indicating that a patient with negative test results for both of these variables still has about a 14% chance of actually being infected.

The model developed in the present study is similar to a model developed by Wright et al. using a similar method, with the exception of hematuria, which was not statistically significant using our data, and dysuria, which was not considered in developing our model. It has been shown that any criterion used to indicate a disease state has a higher sensitivity when only symptomatic patients are screened with the criteria. This suggests that incorporation of symptoms manifested by the patient into criteria increases the sensitivity and specificity of the criteria. However, this may not be a practical addition to an algorithm if the urinalysis is not performed in the physician’s office. If a clinical laboratory performs the urine testing, the patient’s symptoms may not be known, as was the case in the present study.

The predictive values based on the presence of at least moderate numbers of bacteria were similar to results of Zaman et al. However, Lohr et al. found a lower positive predictive value but a much higher negative predictive value based on the presence of bacteria. This finding may have been due to the inclusion of Gram-stained urinary sediment slides in addition to unstained slides. The positive and negative predictive values of the leukocyte esterase found in the
present study were similar to results found by Males et al\textsuperscript{7} when testing similar patient populations.

When all of the variables were tested individually for relationship to infection (Table 2), none were statistically significant except those present in the final model, with the exception of presence of WBCs and nitrite. The presence of leukocyte esterase was related very strongly to the presence of WBCs. Therefore, when the presence of leukocyte esterase was controlled for, the presence of WBCs as demonstrated microscopically did not add additional information and, therefore, was not statistically significant in the final model.

The nitrite result is a well-recognized indicator of infection. When tested alone, nitrite was related to infection ($P = 0.019$). However, the nitrite result was discarded as not statistically significant during the model creation phase. This may be due to the insensitivity of the nitrite test to detect nitrate-reducing microorganisms in the present study. Of the cultures that contained clinically significant nitrate-reducing organisms, 78.9\% were negative in the nitrite test. This may have been caused by the urine not remaining in the bladder long enough for the organisms to reduce nitrate to nitrite, the patient not having enough dietary nitrate, or reduction of the nitrite to nitrogen or ammonia. This supports findings by other similar studies.$^{2,3,8}$

Based on the results in the present study, the urinalysis is not a sufficiently strong predictor of urinary tract infection to be relied on as a sole test. The negative predictive value is too low to permit the physician to confidently rule out urinary tract infection, while the positive predictive value is too low to confirm diagnosis of a urinary tract infection. This seems to be contradicted by the strong statistical significance
of the models developed. However, a strong statistical relationship does not necessarily mean that the relationship is strong enough to be relied on for diagnostic purposes.

Some studies have reached different conclusions. Orenstein and Wong\(^9\) reported that in cases of uncomplicated urinary tract infection in women, urine culture and sensitivity is not necessary owing to the predictable nature of the pathogens and their susceptibility patterns. However, several studies\(^{10-12}\) have noted increasing resistance among common urinary tract pathogens and recommend the use of antimicrobial testing to assure that proper antibiotics are chosen. In addition, urine cultures are used to confirm a diagnosis of urinary tract infection. Given the low positive predictive values calculated in the present study, the use of leukocyte esterase or microscopic examination alone to determine the presence of infection would have resulted in unnecessary administration of antimicrobial agents to one third to one half of the treated patients. For this reason, culture is still the definitive test to determine whether a urinary tract infection is present. Using culture results will assure that the patient receives the proper antimicrobial therapy or that the patient does not receive unnecessary treatment.

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References