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BRIEF REPORT

Performance of Urinalysis Parameters in Predicting Urinary Tract Infection: Does One Size Fit All?

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In a multihospital cohort study of 3392 patients, positive urinalysis parameters had poor positive predictive value for diagnosing urinary tract infection (UTI). Combined urinalysis parameters (pyuria or nitrite) performed better than pyuria alone for ruling out UTI. However, performance of all urinalysis parameters was poor in older women.

Keywords. pyuria; leukocyte esterase; nitrite; reflex urine cultures; diagnostic stewardship.

The urinalysis (UA) is a popular screening test used across inpatient and outpatient clinical settings. The extensive use of UA in patients without suspicion of urinary tract infection (UTI) leads to identification of UA parameters like pyuria or presence of nitrite, which in turn triggers urine cultures, inappropriate antimicrobial use, and associated harms like *Clostridioides difficile* infection [1].

On recent surveys of academic and community hospitals, almost 50% of hospital laboratories used reflex urine culture approaches (also referred to as UA with reflex to culture) [2, 3]. In this approach, when specific UA parameters (eg, leukocyte esterase, white blood cells [WBC], or bacteria) are positive, alone or in combination, the specimen is automatically processed for urine culture [4]. However, performance of UA parameters in predicting UTI has not been systematically investigated or validated for different populations [5]. Additionally, many prior investigations of UA have focused on microbiological outcomes (bacteriuria), which does not confirm presence of infection [6].

Our objectives were to (1) compare the performance of different UA parameters (alone and in combination) in predicting UTI and (2) to stratify this performance based on age and sex. More importantly, the overall goal of this study was to provide guidance to clinicians and laboratories on how to interpret urinalysis in patients with suspicion for UTI [3, 7–9].

METHODS

Study Design and Setting

This retrospective cohort study was conducted across 5 study hospitals (1 academic medical center, 4 community hospitals) in 3 states (North Carolina, Virginia, Georgia). We excluded sites that did not perform microscopic urinalysis or performed reflex urine culture orders due to variability in reflex criteria and in keeping with our goal to assess patients who received urine tests based on clinical suspicion. This study was considered exempt by Duke University Health System Institutional Review Board (protocol number 00107418) and all other participating sites.

Study Population

This study included adult patients if (1) they were hospitalized or seen in the emergency department of 1 of the 5 study hospitals between 1 January 2017 and 31 December 2019, and (2) received UA and urine culture order within 24 hours of each other. Exclusion criteria included age <18 years and presence of an indwelling urinary catheter. Duplicate or repeat patient encounters were also excluded. A random number generator was used to select patient encounters from each site for chart review.

Chart Review Process

Trained abstractors (M. R., J. D., H. T., R. J., Y. R., A. F., S. A., A. H., S. P., and F. M.) collected data from selected patients into a 60-question electronic REDCap survey (Supplementary Data 1). Objective data on demographics, laboratory, and radiographic findings was abstracted from medical records. Signs and symptoms were collected from documented vitals and clinician and nursing documentation 48 hours before and after urine culture collection. A standardized data dictionary was created. Random audits of 10% of charts were conducted by the lead investigator to ensure data integrity. The lead investigator (S. D. A.) met with abstractors biweekly during the data collection period to review any discrepancies from audits and address questions about the chart review process.

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Table 1. Performance of Individual Urinalysis Parameters in Predicting Urinary Tract Infection (N = 3392)

Parameter	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Leukocyte esterase (n = 3346)				
≥Trace LE	0.90 (.88–.93)	0.49 (.47–.51)	0.33 (.31–.35)	0.95 (.94–.96)
≥1+ LE	0.88 (.86–.91)	0.50 (.48–.52)	0.33 (.30–.35)	0.94 (.93–.95)
≥2+ LE	0.21 (.18–.24)	0.80 (.79–.82)	0.23 (.20–.26)	0.79 (.77–.80)
Pyuria WBCs/hpf (n = 3230)				
≥5	0.92 (.90–.94)	0.43 (.42–.45)	0.32 (.30–.34)	0.95 (.94–.96)
≥10	0.84 (.81–.86)	0.55 (.54–.57)	0.35 (.33–.37)	0.92 (.91–.94)
≥20	0.70 (.67–.74)	0.66 (.65–.68)	0.37 (.35–.40)	0.89 (.87–.90)
Nitrite (n = 3384)				
Positive	0.48 (.45–.52)	0.83 (.82–.84)	0.43 (.40–.47)	0.86 (.84–.87)
Bacterial count/hpf (n = 3249)				
5–50	0.20 (.18–.23)	0.77 (.75–.79)	0.20 (.17–.23)	0.77 (.76–.79)
>50	0.72 (.69–.75)	0.71 (.69–.73)	0.41 (.39–.44)	0.90 (.89–.91)

Abbreviations: CI, confidence interval; hpf, high-power field; LE, leukocyte esterase; NPV, negative predictive value; PPV, positive predictive value; WBC, white blood cell.

Table 2. Single-Parameter Negative Predictive Values With 95% Confidence Intervals by Age and Sex

	NPV (95% CI)				
Sex and Age Group	≥ Trace LE	≥1+ LE	≥5 WBCs/hpf	≥10 WBCs/hpf	Nitrite Positive
Female <65 y (n = 872)	0.93 (.90–.96)	0.92 (.89–.95)	0.91 (.88–.95)	0.90 (.86–.93)	0.84 (.81–.87)
Female ≥65 y (n = 1149)	0.90 (.87–.94)	0.89 (.85–.92)	0.92 (.89–.95)	0.87 (.84–.90)	0.81 (.78–.84)
Male <65 y (n = 604)	0.98 (.97–1.00)	0.98 (.97–1.00)	0.97 (.95–.99)	0.97 (.95–.98)	0.92 (.90–.95)
Male ≥65 y (n = 767)	0.98 (.96–.99)	0.97 (.96–.99)	1.00 (.99–1.00)	0.98 (.96–.99)	0.88 (.85–.90)

Abbreviations: CI, confidence interval; hpf, high-power field; LE, leukocyte esterase; NPV, negative predictive value; WBC, white blood cell.

Our outcome of interest was "UTI," defined [10] as bacterial growth of >100 000 colony-forming units per milliliter (CFU/mL) in the urine of patients with any genitourinary signs or symptoms or presence of at least 2 of the following without other cause: fever, rigors, hypotension, nausea or vomiting, delirium, or new urologic obstruction or trauma causing bleeding.

Analysis

We evaluated the performance of relevant UA parameters (pyuria, nitrite, leukocyte esterase, bacteria) in predicting UTI by assessing sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV). We also combined 18 different UA criteria (Supplementary Figure 1, Supplementary Data 2) and used the area under the receiver operating characteristic curve (AUROC) to identify the 5 best-performing models. We further assessed the NPV of pyuria, leukocyte esterase, and nitrite across different groups: male versus female, and age <65 versus ≥65 years. We also performed subanalyses for (1) outcome of UTI as defined by the Infectious Diseases Society of America (IDSA), (2) growth of *Escherichia coli* in urine culture, and (3) clean catch collection methods.

RESULTS

During the study period, 220 531 encounters met study criteria. After using a random number generator and removing duplicates, 3392 encounters were included for analysis. Median age across the entire cohort was 67 years (interquartile range, 54–79 years), and 2021 (59.6%) patients were female. Of the 3392 patient encounters, 1427 (42.1%) urine cultures grew organisms ≥100 000 CFU/mL, 1038 (30.6%) were negative or grew normal urogenital flora, 578 (17%) grew mixed flora, and 349 (10.3%) grew 1000–99 999 CFU/mL. Of positive urine cultures, 44.1% grew *Escherichia coli*. Forty-one percent of urine cultures were obtained in the emergency department (only 3 met outpatient criteria), 46.3% from medical or surgical wards, and 6.8% from intensive care units.

In this cohort, 723 (21.3%) patients met criteria for UTI. No single UA parameter had high sensitivity (≥95%) for UTI. Even though trace leukocyte esterase and low-level pyuria (≥5 white blood cells/high-power field [WBCs/hpf]) had reasonable sensitivity (≥90% for both), this sensitivity decreased with increasing levels of pyuria and leukocyte esterase. When examining UA parameters for their NPV, absence of trace leukocyte esterase and pyuria (≥5 WBCs/hpf) had a high NPV (≥95%; Table 1) for UTI. Subanalyses for IDSA definition of UTI and clean collection methods show similar results with slightly higher NPV (Supplementary Data 3). However, NPV of pyuria, leukocyte esterase, and nitrite differed based by age and sex, with poor utility in older women (Table 2).

Table 3. Complete Performance Estimates for the 5 Models With the Best Area Under the Receiver Operating Characteristic Curve Performance

Model	Test Rule	AUROC	NPV (95% CI)
Model 6 (n = 3231)	≥20 WBCs/hpf or nitrite	0.7093	0.92 (.91–.94)
Model 1 (n = 3347)	≥Trace LE or nitrite	0.7069	0.97 (.96–.98)
Model 5 (n = 3231)	≥10 WBCs/hpf or nitrite	0.7061	0.95 (.94–.96)
Model 2 (n = 3347)	≥1+ LE or nitrite	0.7039	0.96 (.95–.97)
Model 9 (n = 3207)	≥2+ LE or ≥20 WBCs/hpf or nitrite	0.6866	0.95 (.93–.96)
Single parameters	≥Trace LE	0.6987	0.94 (.93–.95)
	≥1+ LE	0.6918	0.95 (.94–.96)
	≥5 WBCs/hpf	0.6768	0.95 (.94–.96)
	≥10 WBCs/hpf	0.6962	0.92 (.91–.94)
	Nitrite positive	0.6565	0.86 (.84–.87)

In this cohort, 723 (21.3%) patients met criteria for urinary tract infection (UTI), and 2669 (78.7%) did not have a UTI.

Abbreviations: AUROC, area under the receiver operating characteristic curve; CI, confidence interval; hpf, high-power field; LE, leukocyte esterase; NPV, negative predictive value; WBC, white blood cell.

The models using combined UA parameters (model 5 [pyuria ≥10 WBCs/hpf or nitrite] or model 2 [1+ leukocyte esterase or nitrite]) performed better in ruling out UTI compared to pyuria alone (Table 3). If either of these models were used as cut-offs for ordering urine cultures, 1244 (46.6%) and 1272 (47.6%) urine cultures, respectively, would have been avoided in patients without UTI, and <5% would have been missed in patients with suspicion for UTI (majority in older women).

DISCUSSION

In this cohort study of 3392 patients who received urine tests for suspicion of UTI, all UA parameters, alone or in combination, had poor PPV for the diagnosis of UTI. However, absence of urinalysis parameters (eg, pyuria) had a high NPV for ruling out UTI. Additionally, both NPV and PPV of all UA parameters were low in older women, likely due to contamination or colonization [11]. Most importantly, combined urinalysis parameters (pyuria or nitrite) performed better than pyuria alone for ruling out UTI, especially in men and in patients <65 years of age. If hospital laboratories leveraged combined UA criteria (1+ leukocyte esterase or nitrite OR pyuria ≥10 WBCs/hpf or nitrite) for their NPV, almost half of unnecessary urine culture orders can be avoided.

Our study also highlights the poor performance of commonly used pyuria thresholds (≥5, ≥10, ≥20 WBCs) in reflex urine culture protocols [2–4]. One prior study showed that higher degree of pyuria should be considered when evaluating older women for UTI [5]. However, our study showed that sensitivity of pyuria in diagnosing UTI decreased with increasing levels of pyuria. These differences can likely be explained by our patient population (hospitalized patients) and evaluating UA performance using real-world experiences with urine culture ordering and collection. This is an important finding as increasing levels of pyuria drive inappropriate antimicrobial prescribing, even in asymptomatic hospitalized inpatients [1].

Hence, a concerted effort should be made to reduce reliance on positive UA parameters as the sole criteria to order urine cultures. This can be done by limiting the use of reflex urine culture protocols to symptomatic patients and developing clinical decision support tools to avoid urine testing in asymptomatic patients. Another alternative would be to use conditional urine cultures, where both UA and urine culture are simultaneously ordered, but the urine culture is canceled based on UA criteria. Second, even when leveraged for their NPV, UA parameters vary based on the patient characteristics: male versus female patients, symptomatic versus asymptomatic patients, or older versus younger patients. Hence, reflex urine cultures or clinical decision support tools should incorporate appropriate exclusion criteria based both on patient population (eg, neutropenic patients) and markers of contamination (eg, squamous cells) [6].

We acknowledge the inherent limitations of our retrospective design, chart review process, and generalizability as we examined data from hospitals in the southeastern United States. We also did not include pediatric, catheterized, or outpatient clinic populations. In the absence of patient-specific antibiotic use data, we could not exclude patients who received prior antibiotics. Additionally, our definition of UTI was based on expert panel discussions, as there is no consistent definition across infectious disease and urologic societies [12, 13].

Most guidelines and antibiotic stewardship interventions focus on urine cultures, but UA is an important precursor test that needs to be targeted for diagnostic stewardship [1]. Additionally, UA performance varies across patient populations and laboratories, which highlights the need for site-specific assessment. We need to educate clinicians about the poor PPV of positive UA parameters to decrease reliance on UA for diagnosing UTIs, especially in older adults. Future reflex urine culture workflows and urine culture stewardship interventions should leverage UA for its NPV and prioritize populations where the absence of pyuria indicates a low likelihood of UTI [6].

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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