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Sensitivity and specificity of urinalysis samples in critically ill patients

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Abstract

Background: Pre-emptive screening of urine for patients admitted to an intensive care unit can result in the misinterpretation of data and over- or under-treatment of urinary tract infection.

Methods: Data were studied from 169 consecutive patients admitted to the neurologic or burn intensive care unit at Shands Hospital at the University of Florida. All patients had a urinary catheter in place at the time of admission. Urinalysis and urine culture were sent for analysis. Data included leukocyte esterase, urine nitrate, urine protein, pyuria or urine white blood cell count, and culture.

Results: Leukocyte esterase and pyuria were the most sensitive indicators of a positive urine culture at 87.5% (95% CI: 71.3–100%) and 73.3% (95% CI: 51.0–95.7%), respectively; urine nitrate was specific at 100%. More than half of the patients (56.3%) with positive cultures did not initially receive antibiotics.

Conclusion: The combination of leukocyte esterase and urine nitrate provides the best indicator for the initiation of antibiotic coverage for urinary tract infection prior to culture availability.

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Key words: urinary tract infection; leukocyte esterase; urine nitrate; urine white blood cell count; urine protein

Hospital-acquired infections (HAI) represent a significant economic and public health burden to the American healthcare system. Estimates indicate that approximately 99,000 patients die each year from an HAI illness, with an annual cost ranging from 4.5 to 11 billion American dollars [1]. The leading cause of HAI is catheter-associated urinary tract infection, accounting for 40% of all nosocomial infections [2]. In 2008, as an incentive for hospitals to improve their infection-control practices and avoid financial loss, Medicare ceased reimbursing hospitals for procedures resulting in certain HAIs, including hospital-acquired catheter-associated urinary tract infection [3]. This has caused some institutions to implement policies that pre-emptively screen for infection on admission, regardless of whether the patient exhibits any signs or symptoms related to targeted organ system infection. The public health and economic ramifications of these pre-emptive screening strategies have yet to be examined in detail. There are concerns, however, that widespread screening could result in unintended consequences, such as patient-selection bias and the overuse of antibiotics, which leads to antibiotic resistance [4].

Critically ill patients, especially those who are mechanically ventilated, are frequently catheterized for the purposes of monitoring fluid status and relieving bladder congestion. These patients fail to develop the classical manifestations of urinary tract infection (pain, dysuria, urgency, fever, and leukocytosis) even when urine culture results are positive [5]. In these instances, a positive urine culture itself often prompts the initiation of antibiotic therapy. As the urine culture result may take several days, urinalysis is frequently relied upon to predict urine culture growth and for the initiation of early antibiotics. Protocol-driven urine screening can increase the number of urinalysis samples being sent, while correct interpretation of urinalysis has become more important.

The utility of urinalysis to predict urine culture growth has been extensively studied in outpatient and emergency department settings. Although leukocyte esterase has a reported sensitivity of 50% to 97%, its specificity is only 41% to 86%. Abnormal nitrite demonstrates greater specificity

(92% to 100%), but suffers from poor sensitivity (19% to 48%). Similar to leukocyte esterase, pyuria (≥ 5 WBCs per hpf) also has a high sensitivity (94% to 100%), but poor specificity (47% to 50%). Microscopic haematuria and proteinuria are of limited utility as they demonstrate only intermediate sensitivity and specificity [6–8]. In a context where history and physical examination often prompt diagnostic testing, however, this can lead to selection bias and affect results. Few studies have evaluated the utility of urinalysis components to predict urine culture results in the intensive care unit (ICU) setting, where history and physical exams are limited at best, as patients are critically ill or unable to communicate.

In this study, we investigated how well various components of urinalysis in the ICU setting were able to predict urine culture results. We also performed a secondary analysis to determine how frequently antibiotics were started appropriately in anticipation of a positive culture result, and the incidence of inappropriate antibiotic exposure in relation to a negative culture. We further examined the various aspects of the urinalysis that were drivers of antibiotic initiation.

METHODS

PATIENTS AND SETTING

The study protocol was approved by our university's Institutional Review Board. Written consent was waived for this review. This was a retrospective cohort study of all catheterized patients directly admitted to the neurological ICU and the burn ICU at our university from January 1, 2012 to June 30, 2014. The neurosurgical ICU is a 30-bed unit that admits peri-operative neurosurgical patients, patients with aneurysmal subarachnoid haemorrhage, stroke patients of a haemorrhagic or ischaemic nature, and those with seizures or neuromuscular disorders. The burn ICU is an eight-bed ICU that is the only designated burn facility serving the entire North Florida and South Georgia regions. In the neurological ICU, patients are managed by the critical care team along with the respective neurosurgery or neurology team. The critical care team in the burn ICU manages the patients, along with the burn service team.

In the neurosurgical ICU, if patients are mechanically ventilated secondary to their primary neurological insult, they are routinely catheterized. Our institutional protocol calls for a urinalysis and urine culture to be sent after catheterization, with the decision to initiate antibiotic therapy based on the urinalysis result. Patients in the burn ICU are catheterized if they have large surface area burns covering > 15% total body surface area to guide fluid resuscitation, or if they require mechanical ventilation.

Patients older than 18 years old admitted to the respective ICUs from January 1, 2012 to June 30, 2014 who had a catheterized urinalysis and urine culture sent as part of their initial evaluation were included in the analysis. The presence or absence of fever, abdominal pain, dysuria, prior catheterization, prior antibiotics, oliguria, and pregnancy did not influence inclusion and were not recorded.

Treatment of presumed urinary tract infection based on urinalysis was at the sole discretion of the ICU teams. Antibiotics routinely administered for peri-operative prophylaxis did not exclude a patient from the study and were not recorded.

We defined a positive urine culture as $\geq 10^5$ CFU mL^{-1} of pathogenic bacteria, with fewer than two species present, which is also the Centers for Disease Control definition [9]. Components of the urinalysis including leukocyte esterase, nitrite, white blood cell count (WBC), red blood cell count (RBC), protein, and bacteria were compared to final culture results. At our institution, leukocyte esterase and bacteria are respectively reported as ordinal results (negative, trace, small, moderate, and large, and none, rare, few, occasional, moderate, and many). To analyze our data in a binary manner, we dichotomized leukocyte esterase into two groups, namely: negative, and those with any amount of leukocyte esterase activity. Bacteria were similarly divided into none and those with the presence of any number of bacteria. Protein is reported in descriptive and numerical terms with ordinal gradation (increasing from negative to trace, then from 30 to 300 mg dL^{-1}). We dichotomized protein into two groups of negative and those with any degree of positivity. WBC and RBC are reported as ordinal variables with discrete values which were analyzed as two groups (WBC 0 ≤ 4 per hpf and WBCs ≥ 5 per hpf, and RBC 0 ≤ 4 per hpf and RBCs ≥ 5 per hpf), respectively. Urinalysis samples were analysed on an Arkray AZ-4280 (Arkray USA, Minneapolis, MN) analyser that is tested against College of American Pathologists standards.

A statistical analysis was performed using JMP 12.0 (SAS Institute, Cary, NC). Measures were summarized as mean and standard deviations (continuous) and percentages (categorical). Associations between measures were calculated using chi-square analysis. Contingency tables created from these analyses were then used to calculate odds ratios, sensitivity, and specificity, with 95% confidence intervals (CI) estimated for each of these metrics. $P < 0.05$ was considered statistically significant.

RESULTS

Samples from 169 patients were included for analysis (Table 1). Fifteen patients did not have a WBC analysis and 14 had no results for RBCs. Males and females were equally represented, with a mean age of 51 years. Urine culture was positive in 9.5% (16/169) of patients. The mean age of patients with a positive culture was older than the negative culture group (59.6 ± 10.6 vs. 50.5 ± 13.0; $P = 0.005$).

Table 1. Patient demographics, urinalysis results, and database characteristics

	Number (%)	Mean (SD)
Number of patients	169	
Age (years)		51.4 (13.0)
Female	85 (50.3%)	
Male	84 (49.7%)	
Positive culture	16 (9.5%)	
Leukocyte esterase		
large	13 (7.7%)	
moderate	12 (7.1%)	
small/trace	32 (18.9%)	
negative	112 (66.3%)	
Nitrite-positive	4 (2.4%)	
protein		
large (> 100 mg dL^{-1})	15 (8.9%)	
moderate (30–100 mg dL^{-1})	33 (19.6%)	
trace (10–30 mg dL^{-1})	26 (15.5%)	
negative	94 (56.0%)	
		13.0 (46.3)
WBC > 5 per hpf	50 (29%)	
		28.4 (100.6)
RBC > 5 per hpf	64 (37%)	
Bacteria present	19 (11.2%)	
Fever (temp > 38.5°C)	25 (14%)	
Antibiotics started	39 (23%)	

Raw data are presented as number (%) or mean (SD); SD — standard deviation; hpf — high power field

Although urine samples were obtained from catheterized specimens in 78.0% of admitted patients, there was no association between catheterized specimens and culture positivity ($P = 0.77$). The presence of a fever > 38.5°C was also not associated with culture positivity ($P = 0.64$).

Leukocyte esterase and pyuria > 5 WBC/hpf were the most sensitive indicators for culture positivity: 87.5% (95% CI: 71.3–100%) and 73.3% (95% CI: 51.0–95.7%), respectively (Table 2). Urinary nitrite was perfectly specific at 100%. Other components only revealed intermediate sensitivity and specificity, which are further described in Table 3.

We also examined how well urinalysis results were interpreted. Of the patients, 56.3% with positive cultures did not have antibiotics initially started. Those patients (20.2%) with negative cultures received empiric antibiotics based on the urinalysis (Table 4). Healthcare providers relied strongly on nitrite positivity ($P < 0.001$), WBC > 5 ($P < 0.001$), and the presence of bacteriuria ($P = 0.003$) as decision-making drivers to initiate antibiotics.

DISCUSSION

Prior studies on the test characteristics of urinalysis were mostly performed in an outpatient or emergency department setting, where history and physical findings influence patient selection. Our study focused on unselected ICU patients with the hypothesis that without history or physical findings to influence patient selection, urinalysis test characteristics would need to be interpreted differently. In our burn ICU and neurological ICU patients, the sensitivity and specificity of urinalysis components are consistent with what has been reported in the literature. In this study, four urinalysis components (leukocyte esterase, nitrite, WBC, and bacteria) had sufficient discriminatory value to be useful. We found that leukocyte esterase was 82.6% sensitive, consistent with the 50% to 97% sensitivity as previously reported. Urinary nitrite was 100% specific, which is also consistent with 92% to 100% specificity as previously indicated. The combination of leukocyte esterase and urinary nitrite could be used as an accurate, robust indicator for positive bacteria cultures. For other measures, pyuria with WBCs >5 per hpf was 72.7% sensitive for culture positivity, which is also within the range of 69% to 90% sensitivity as previously reported [6, 10]. We found that bacteriuria was 92.9% specific, within the range of 89% to 94% from prior studies [6].

At our institution, the decision to start antibiotics based on urinalysis is often made by junior residents and advanced practice providers with varying years of experience. Our institution does not require the attendance or approval of a pharmacist for routine antibiotic initiation. This study also did not explicitly examine the training level or experience of the person ordering antibiotics because, as often happens in a team environment, the ordering provider may not necessarily be the decision maker. We found that over half of the patients with positive cultures did not have antibiotics initiated, and that nearly one in five patients with a negative culture received antibiotics inappropriately. Whether this represents clinical decisions based on uncaptured data such as urine appearance, clinical course, urine odour, systemic leukocytosis, culture positivity in another bodily location, or simply an error in test interpretation is unknown. We did find that leukocyte esterase, nitrite, WBCs > 5 per hpf, and the presence of bacteria are useful discriminators. However, healthcare providers used only three out of these four factors in their decision making, essentially ignoring leukocyte esterase. To our knowledge, no other study has examined how well healthcare providers interpret urinalysis, or the factors behind their treatment decisions. Several score-based decision aids have been developed to guide clinicians in predicting culture positivity and antibiotic use [10–13]. Their utility, however, is limited by their poor performance, reliance on history and physical findings, as well as derivation

Table 2. Comparison of factors associated with positive urine cultures

Characteristic	% of patients with Positive cultures	% of patients with Negative cultures	Odds ratio (for positive cultures)	*P*-value
Catheter sample				
yes	12/16 (75.0%)	119/153 (78.3%)	0.88 (0.51–1.65)	0.77
no	4/16 (25.0%)	33/153 (21.7%)		
Leukocyte esterase				
any	14/16 (87.5%)	43/153 (28.1%)	3.84 (2.07–8.78)	< 0.001
negative	2/16 (12.5%)	110/153 (71.9%)		
Nitrite				
positive	4/16 (25.0%)	0/153 (0%)	10.51 (3.30–122.34)	< 0.001
negative	12/16 (75.0%)	153/153 (100%)		
Protein				
any	5/16 (31.2%)	69/153 (45.4%)	0.76 (0.43–1.27)	0.27
negative	11/16 (68.8%)	83/153 (54.6%)		
WBC (> 5 per hpf)				
yes	11/15 (73.3%)	39/139 (28.1%)	2.55 (1.48–4.78)	< 0.001
no	4/15 (26.7%)	100/139 (71.9%)		
RBC (> 5 per hpf)				
yes	9/16 (56.2%)	55/139 (39.6%)	1.39 (0.84–2.35)	0.20
no	7/16 (43.8%)	84/139 (60.4%)		
Bacteria				
any	7/16 (43.8%)	12/153 (7.8%)	3.00 (1.70–5.26)	< 0.001
negative	9/16 (56.2%)	141/153 (92.3%)		
Fever > 38.5°C				
yes	3/16 (20.0%)	22/144 (15.3.0%)	1.23 (0.61–2.23)	0.64
no	12/16 (80.0%)	122/144 (84.7.0%)		

Raw data are presented as number (%); CI — confidence interval; LE — leukocyte esterase; WBC — white-blood-cell count; hpf — high power field

Table 3. Clinical validity for predicting positive cultures.

	Sensitivity	Specificity
Catheter use	75.0%	21.7%
	53.8–96.2%	15.2–28.3%
LE	87.5%	71.9%
	71.3–100%	64.8–79.0%
Nitrite	25.0%	100%
	3.8–46.2%	100–100%
WBC	73.3%	71.9%
	51.0–95.7%	64.5–79.4%
RBC	56.3%	60.4%
	31.9–80.6%	52.3–68.6%
Protein	31.3%	54.6%
	8.5–54.0%	46.7–62.5%
Bacteria	43.8%	92.2%
	19.4–68.1%	87.9–96.4%

White blood cells and red blood cells were considered present if greater than 5 per hpf. LE, protein, and bacteria were considered present if the results showed any degree of positivity; LE — leukocyte esterase; WBC — white-blood-cell count; CI — confidence interval; RBC — red-blood-cell count; hpf — high power field

of information from patients in ambulatory settings. While the aim of our study was not to develop such a scoring system, we showed that when two urinalysis indicators were combined, their cumulative predictive value improved dramatically. Further work on such a scoring system could prove very useful.

Our work has several important limitations. First, we make the assumption that culture positivity equals urinary tract infection and do not distinguish asymptomatic bacteriuria. Asymptomatic bacteriuria is common, with a prevalence that varies widely from 1% to > 20% of women residing in the community, and from 3% to 19% among elderly men in the community [14, 15]. Large prospective studies have shown that untreated asymptomatic bacteriuria has no impact on renal function, number of symptomatic urinary tract infections, or mortality. Indeed, Infectious Diseases Society of America guidelines recommend against testing for or treating asymptomatic bacteriuria, except for pregnant patients or those undergoing urological procedures [16]. The guidelines offer no counsel for ICU patients, however, and thus far no studies have evaluated the clinical impact

Table 4. Factors associated with starting antibiotics

Characteristic	% of patients with antibiotics started	% of patients with no antibiotics started	Odds ratio (for antibiotics started)	*P*-value
Catheter sample				
yes	31/39 (79.5%)	100/130 (77.5%)	1.05 (0.69–1.64)	0.79
no	8/39 (20.5%)	29/130 (22.5%)		
Leukocyte esterase				
any	24/39 (61.5%)	33/130 (25.4%)	2.14 (1.48–3.15)	< 0.001
negative	15/39 (38.5%)	97/130 (74.6%)		
Nitrite				
positive	4/39 (10.3%)	0/130 (0%)	5.75 (1.84–66.51)	< 0.001
negative	35/39 (89.7%)	130/130 (100%)		
Protein				
any	21/39 (53.9%)	53/130 (41.1%)	1.29 (0.90–1.84)	0.16
negative	18/39 (46.2%)	76/130 (58.9%)		
WBC (> 5 per hpf)				
yes	24/38 (63.2%)	26/116 (22.4%)	2.40 (1.64–3.59)	< 0.001
no	14/38 (36.8%)	90/116 (77.6%)		
RBC (> 5 per hpf)				
yes	20/35 (57.1%)	44/120 (36.7%)	1.51 (1.04–2.22)	0.03
no	15/35 (42.9%)	76/120 (63.3%)		
Bacteria				
any	10/39 (25.6%)	9/130 (6.9%)	2.13 (1.31–3.49)	0.003
negative	29/39 (74.4%)	121/130 (93.1%)		
Fever > 38.5°C				
yes	6/39 (15.8%)	19/120 (25.4%)	1.01 (0.36–2.56)	0.95
no	33/391 (84.2%)	101/120 (84.6%)		

of untreated asymptomatic bacteriuria on the critically ill. Furthermore, it may be impossible to establish the asymptomatic state in critically ill patients with altered mental status, limited examination, and myriad reasons for fever or leukocytosis.

CONCLUSIONS

In conclusion, our study demonstrated no appreciable difference in the sensitivity and specificity of leukocyte esterase, nitrite, WBC, and bacteria in ICU patients as compared to other settings. The interpretation of urinalysis in order to determine infection appeared to be inconsistent, however. This resulted in patients being exposed to unnecessary antibiotics and the absence of treatment in patients who would have benefitted from such therapy. A score-based clinical decision aid may assist one in the interpretation of urinalysis.

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References:

1. Klevens RM, Edwards JR, Richards CL, et al. Estimating health care-associated infections and deaths in U.S. hospitals, 2002. Public Health Rep. 2007; 122(2): 160–166, doi: 10.1177/003335490712200205, indexed in Pubmed: 17357358.
2. Warren JW. The catheter and urinary tract infection. Med Clin North Am. 1991; 75: 481–493.
3. Peasah SK, McKay NL, Harman JS, et al. Medicare non-payment of hospital-acquired infections: infection rates three years post implementation. Medicare Medicaid Res Rev. 2013; 3(3), doi: 10.5600/mmrr.003.03.a08, indexed in Pubmed: 24753974.
4. Burke JP. Infection control - a problem for patient safety. N Engl J Med. 2003; 348(7): 651–656, doi: 10.1056/NEJMhpr020557, indexed in Pubmed: 12584377.
5. Tambyah PA, Maki DG. Catheter-associated urinary tract infection is rarely symptomatic: a prospective study of 1,497 catheterized patients. Arch Intern Med. 2000; 160(5): 678–682, indexed in Pubmed: 10724054.
6. Simerville JA, Maxted WC, Pahira JJ. Urinalysis: a comprehensive review. Am Fam Physician. 2005; 71(6): 1153–1162, indexed in Pubmed: 15791892.
7. Pfaller MA, Koontz FP. Laboratory evaluation of leukocyte esterase and nitrite tests for the detection of bacteriuria. J Clin Microbiol. 1985; 21(5): 840–842, indexed in Pubmed: 3998118.
8. Meister L, Morley EJ, Scheer D, et al. History and physical examination plus laboratory testing for the diagnosis of adult female urinary tract infection. Acad Emerg Med. 2013; 20(7): 631–645, doi: 10.1111/acem.12171, indexed in Pubmed: 23859578.
9. Centers for Disease Control and Prevention: August 24, 2015 Urinary Tract Infection (Catheter-Associated Urinary Tract Infection [CAUTI] and Non-Catheter-Associated Urinary Tract Infection [UTI]) and Other

Urinary System Infection [USI]) Events. http://www.cdc.gov/nhsn/PDFs/pscManual/7pscCAUTIcurrent.pdf (24.08.2015).
10. McIsaac WJ, Moineddin R, Ross S. Validation of a decision aid to assist physicians in reducing unnecessary antibiotic drug use for acute cystitis. Arch Intern Med. 2007; 167(20): 2201–2206, doi: 10.1001/archinte.167.20.2201, indexed in Pubmed: 17998492.
11. Little P, Turner S, Rumsby K, et al. Developing clinical rules to predict urinary tract infection in primary care settings: sensitivity and specificity of near patient tests (dipsticks) and clinical scores. Br J Gen Pract. 2006; 56(529): 606–612, indexed in Pubmed: 16882379.
12. Dobbs FF, Fleming DM. A simple scoring system for evaluating symptoms, history and urine dipstick testing in the diagnosis of urinary tract infection. J R Coll Gen Pract. 1987; 37(296): 100–104, indexed in Pubmed: 3316637.
13. Little P, Turner S, Rumsby K, et al. Validating the prediction of lower urinary tract infection in primary care: sensitivity and specificity of urinary dipsticks and clinical scores in women. Br J Gen Pract. 2010; 60(576): 495–500, doi: 10.3399/bjgp10X514747, indexed in Pubmed: 20594439.
14. Hooton TM, Scholes D, Stapleton AE, et al. A prospective study of asymptomatic bacteriuria in sexually active young women. N Engl J Med. 2000; 343(14): 992–997, doi: 10.1056/NEJM200010053431402, indexed in Pubmed: 11018165.
15. Bengtsson C, Bengtsson U, Björkelund C, et al. Bacteriuria in a population sample of women: 24-year follow-up study. Results from the prospective population-based study of women in Gothenburg, Sweden. Scand J Urol Nephrol. 1998; 32(4): 284–289, indexed in Pubmed: 9764457.
16. Nicolle LE, Bradley S, Colgan R, et al. Infectious Diseases Society of America, American Society of Nephrology, American Geriatric Society. Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. Clin Infect Dis. 2005; 40(5): 643–654, doi: 10.1086/427507, indexed in Pubmed: 15714408.

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