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Kap Sum Foong
University of Illinois

Satish Munigala
Washington University School of Medicine in St. Louis

Ronald Jackups
Washington University School of Medicine in St. Louis

Melanie L Yarbrough
Washington University School of Medicine in St. Louis

Carey-Ann D. Burnham
Washington University School of Medicine in St. Louis

See next page for additional authors

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Incidence and Diagnostic Yield of Repeat Urine Culture in Hospitalized Patients: an Opportunity for Diagnostic Stewardship

Kap Sum Foong,[a] Satish Munigala,[b] Ronald Jackups, Jr.,[c] Melanie L. Yarbrough,[c] Carey-Ann D. Burnham,[c] David K. Warren[b]

[a]Section of Infectious Diseases, Department of Medicine, University of Illinois College of Medicine, Peoria, Illinois, USA
[b]Division of Infectious Diseases, Department of Medicine, Washington University School of Medicine, St. Louis, Missouri, USA
[c]Department of Pathology and Immunology, Washington University School of Medicine, St. Louis, Missouri, USA

ABSTRACT There is limited knowledge on the incidence, diagnostic yield, and cost associated with inappropriate repeat urine cultures. The factors that affect repeat urine culturing practices are not well understood. We conducted a retrospective study of adult inpatients who had ≥1 urine culture performed during their hospitalization between January 2015 and February 2018. We analyzed the proportion of inappropriate repeat urine cultures performed <48 h after the index culture. We defined an inappropriate repeat urine culture to be a repeat urine culture performed following a negative index culture or a repeat urine specimen obtained from the same urinary catheter. Overall, 28,141 urine cultures were performed on 21,306 patients. There were 2,060 (7.3%) urine cultures repeated in <48 h. Of these, 1,120 (54.4%) urine cultures were inappropriate. Predictors for inappropriate repeat urine cultures included collection of the initial urine sample for culture in the emergency department (adjusted odds ratio [aOR], 5.65; 95% confidence interval [CI], 4.70 to 6.78), male gender (aOR, 1.61; 95% CI, 1.42 to 1.84), congestive heart failure (aOR, 1.20; 95% CI, 1.03 to 1.38), and a longer hospital stay (aOR, 1.01 per day; 95% CI, 1.00 to 1.01). A patient with an index urine culture obtained from an indwelling catheter (aOR, 0.65; 95% CI, 0.53 to 0.80) was less likely to have an inappropriate repeat culture. Among 1,120 negative index urine cultures, only 4.7% of repeat cultures were positive for bacteriuria. The estimated laboratory charges for inappropriate repeat urine cultures were $16,800 over the study period. Among inpatients, over half of all urine cultures repeated in <48 h were inappropriate. This offers an opportunity for diagnostic stewardship and optimization of antimicrobial use.

KEYWORDS diagnostic stewardship, diagnostic yield, inappropriate testing, urine culture

In recent decades, the overutilization of laboratory testing has been recognized as a prevalent issue in health care. Inappropriate duplicative testing is an important subset of diagnostic test overuse (1). Although duplicative laboratory testing is indicated in some instances, it is often unnecessary and provides limited clinically important information, especially if the laboratory test is repeated in an inappropriately short interval (2, 3).

Urine cultures are among the most frequently performed tests in clinical microbiology laboratories (4). An accurate diagnosis of urinary tract infection is important to identify patients who will benefit from appropriate antimicrobial treatment. However, unnecessary urine culture testing can result in increased health care costs and inappropriate antimicrobial treatment for asymptomatic bacteriuria, which impedes antimicrobial stewardship efforts and can lead to downstream antimicrobial resistance and

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Address correspondence to Kap Sum Foong, FoongKS@uic.edu, or David K. Warren, dwarren@wustl.edu.

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Clostridioides difficile infection (5). Utilization practices, the diagnostic yield of repeat urine culture among hospitalized patients, and the factors that affect ordering practices are not well understood.

The purpose of our study was to evaluate the incidence, predictors, diagnostic yield, and economic burden of inappropriate repeat urine cultures performed less than 48 h after the index culture among hospitalized patients. These results have the potential to improve diagnostic test utilization, thereby reducing health care costs and minimizing inappropriate antimicrobial therapy.

MATERIALS AND METHODS

Setting. This was a retrospective study conducted at Barnes-Jewish Hospital, a 1,250-bed teaching hospital, from January 2015 to February 2018. We included all hospitalized patients aged ≥18 years who had at least one urine sample processed by culture during their hospital stay or within 24 h prior to admission.

Definitions. For the purpose of this study, we defined the first urine culture performed during admission or within 24 h prior to admission to be the "initial" culture. A sample for an initial urine culture could be obtained in an outpatient setting (e.g., a clinic, skilled nursing facility, or long-term acute care facility), the emergency department, or an inpatient setting. We defined an "index" urine culture to be the first urine culture performed prior to a repeat urine culture(s). For some of the hospitalized patients, the index urine cultures were also the initial urine cultures.

Based on previous literature (2, 6), we defined a repeat urine culture performed within less than 48 h to be inappropriate if either (i) a repeat urine culture was performed following a negative index culture or (ii) a repeat urine specimen was obtained from the same indwelling urinary catheter. We considered a repeat urine culture to be clinically appropriate if (i) it was repeated for the confirmation of a positive index culture or (ii) a specimen for a repeat catheterized urine culture was obtained from a newly inserted indwelling urinary catheter, given concerns of initial culture contamination from an old urinary catheter (2, 6).

Pertinent data on the patients' demographics, comorbidities, urine cultures (date of collection, type of urine specimen, culture result, ordering service, ordering physician), results of an urinalysis associated with the urine cultures (i.e., results of an urinalysis performed either concomitantly with or within 1 h before the index urine culture), and disposition were extracted from the medical informatics database. The type of urine specimen was classified into clean-catch/straight catheterized, indwelling catheterized (e.g., the specimen was obtained from a Foley or suprapubic catheter), or procedural (e.g., the specimen was obtained by suprapubic aspiration, percutaneous nephrostomy tube placement, or cystoscopy), as indicated by the ordering physician. Due to the low numbers of straight catheterized urine cultures (0.3% of all urine cultures), these were grouped together with clean-catch urine cultures. A positive urine culture for all specimen types was defined on the basis of the established clinical breakpoints, as previously published (7, 8). We defined a negative urine culture as having insignificant growth below a threshold or no growth. A urine culture was considered contaminated if there were ≥3 different species of organisms with colony counts recovered above a threshold. An abnormal urinalysis was defined as a leukocyte esterase value of ≥1 on urine dipstick and >5 white blood cells per high-power field on urine microscopy (9).

The primary study outcome was the proportion of inappropriate repeat urine cultures performed within less than 48 h following the index urine culture among inpatients. The secondary outcomes were the diagnostic yield of inappropriate repeat urine cultures in detecting bacteriuria, predictors, and direct laboratory charges associated with inappropriate repeat urine cultures performed within less than 48 h. The gross charges estimation for a urine culture test was calculated on the basis of the Medicare Clinical Laboratory Fee Schedule, using a national median Medicare payment rate of $15.00 per urine culture (not adjusted to inflation) (10).

Statistical analyses. The unit of analysis in our study was reported on a per admission basis. Baseline characteristics and urine culture data were compared on the basis of inappropriate repeat urine culturing status using the chi-square test, the Fisher exact test, or univariable logistic regression for categorical variables and the Kruskal-Wallis test for continuous variables. To determine the independent predictors associated with inappropriate repeat urine cultures performed within less than 48 h, we performed multivariable logistic regression analysis. All variables with a P value of <0.20 in univariable analysis were considered for entry into the model using forward stepwise regression, with the variable being retained in the final model if the P value was <0.05. The remaining patients in the study without inappropriate repeat urine cultures during their admission (i.e., patients with only one urine culture or patients with an appropriate repeat urine culture) were regarded as the reference group (controls). We also evaluated the effect of urine culture specimen type (index versus initial) and location among the independent predictors of inappropriate repeat urine cultures. For this, random selection of either the index culture or the initial culture for the control group was performed to avoid a selection bias of oversampling of urine cultures performed with specimens collected in the emergency department.

We performed a sensitivity analysis to determine if our results varied on the basis of inappropriate criteria for repeat urine cultures. For this analysis, we considered all repeat urine cultures performed within less than 48 h after the index culture to be inappropriate. Data were analyzed using SAS (version 9.3) software (SAS Institute Inc., Cary, NC). This study was approved by the Human Research Protection Office at Washington University in St. Louis, MO, with a waiver of consent.

RESULTS

A total of 28,141 urine cultures were performed among 21,306 hospitalized patients during the study period. There were 23,224 clean-catch specimens, 97 straight catheterized specimens, 4,567 indwelling catheter specimens, and 253 procedural specimens. Of these, 4,678 (22.0%) patients had more than one urine culture performed, accounting for 11,513 of all urine cultures (4,678 index cultures, 6,835 repeat urine cultures). Among the 4,678 patients with repeat urine cultures, 1,868 (39.9%) had repeat urine cultures performed within 48 h following the index culture. We identified that 1,120 (54.4%) of 2,060 urine cultures were inappropriately repeated within 48 h following the index urine culture. Of all inappropriate repeat testing, the proportion was the highest for patients who had clean-catch index urine cultures (94.5%) and who were admitted to intensive care units (ICUs) (40.2%). Only 53 (4.7%) of 1,120 inappropriate repeat urine cultures performed within less than 48 h had a positive urine culture. Of these, 41.5% were positive for *Enterobacteriaceae*, 18.9% were positive for enterococci, and 17.0% were positive for *Candida* spp.

Baseline demographics were relatively similar between the control group and the groups with inappropriate repeat urine cultures (Table 1). In univariable analysis, patients with inappropriate repeat urine culture testing were more likely to be male (59.1% versus 47.1%, $P < 0.001$), have a sample for the index urine culture obtained in the emergency department or other outpatient settings (16.8% versus 3.6%, $P < 0.001$), and have a longer median length of hospital stay (9 versus 7 days, $P < 0.001$). Index urine cultures were less likely to be of an indwelling catheterized specimen in the inappropriate repeat testing group (10.3% versus 13.6%, $P = 0.002$). There was no difference in the proportion of urinalyses performed in association with the index cultures between the two study groups. The majority of the inappropriate repeat urine cultures were ordered by the same clinical service that ordered the index culture, ranging from 61.5% to 96.1% (Table 2). Notably, 29% ($n = 325$ out of 1,120) of inappropriate repeat urine cultures were ordered by the same physician.

Among inpatients who had at least one urine culture, the independent predictors associated with having an inappropriate repeat urine culture performed within 48 h of the index culture included an initial urine culture performed with a specimen collected in the emergency department (adjusted odds ratio [aOR], 5.65; 95% confidence interval [CI], 4.70 to 6.78), male gender (aOR, 1.61; 95% CI, 1.42 to 1.84), congestive heart failure (aOR, 1.20; 95% CI, 1.03 to 1.38), and a longer hospital stay (aOR, 1.01 per day; 95% CI, 1.00 to 1.01 per day). An index indwelling catheterized urine culture (aOR, 0.65; 95% CI, 0.53 to 0.80) was less likely to be associated with inappropriate repeat testing. In our sensitivity analysis, there were no significant changes in our univariable and multivariable results when we compared all inpatients who had repeat urine cultures performed within less than 48 h, irrespective of their clinical appropriateness criteria (data not shown). The estimated laboratory charges for these inappropriate repeat urine cultures were $16,800 during the 38-month study period.

DISCUSSION

In this retrospective study, we found that, for 7.3% of all inpatient urine cultures, repeat testing was performed within 48 h following an index culture and that 54.4% of these repeated urine cultures were inappropriate, based on previously published criteria. Among inpatients with a negative index urine culture, the diagnostic gain of an inappropriate urine culture repeated within 48 h for detecting bacteriuria was only 4.7%. Several other studies have examined the utility of repeat microbiological cultures among inpatients. However, these studies were performed in the late 1990s, and the landscape of diagnostic test utilization and antimicrobial resistance has changed considerably since that time. A study by Bates et al. found that 26% of the repeat urine, sputum, and stool cultures performed within 36 h were redundant (2). Onderdonk et al. reported that 14.6% of the repeated urine cultures were unnecessary, based on predefined testing frequency criteria (e.g., no more than one urine culture per day) (11). Nevertheless, the proportion of inappropriate inpatient urine cultures repeated in less

TABLE 1 Characteristics and comparison of risk factors for inappropriate repeat urine culture performed within 48 h following the index urine culture among 21,306 inpatients with >1 urine culture[j]

Characteristic	Value for the following patients:				Multivariable analysis	
	All inpatients (n = 21,306)	Inpatients with ≥1 inappropriate repeat urine culture in <48 h (n = 1,040)	Remaining patients[a] (n = 20,266)	P value	aOR (95% CI)	P value
No. (%) of male patients	10,155 (47.7)	615 (59.1)	9,540 (47.1)	<0.001	1.61 (1.42–1.84)	<0.001
Median (IQR) age (yr)	62 (49–72)	61 (49–71)	62 (49–72)	0.175	1.00 (0.99–1.00)	0.088
Median (IQR) length of stay (days)	7 (4–16)	9 (4–20)	7 (4–16)	<0.001	1.01 (1.00–1.01)	<0.001
No. (%) of patients by race				0.339		
White	14,649 (68.8)	729 (70.1)	13,920 (68.7)			
Others[b]	6,657 (31.2)	311 (29.9)	6,346 (31.3)			
No. (%) of patients with the following comorbidities:						
CHF	5,609 (26.3)	305 (29.3)	5,304 (26.2)	0.024	1.20 (1.03–1.38)	0.018
Chronic lung disease	4,762 (22.4)	213 (20.5)	4,549 (22.4)	0.138		
ESRD	897 (4.2)	54 (5.2)	843 (4.2)	0.106		
Cirrhosis	862 (4.0)	39 (3.8)	823 (4.1)	0.620		
Malignancy	3,544 (16.6)	169 (16.3)	3,375 (16.7)	0.733		
HIV infection	67 (0.3)	4 (0.4)	63 (0.3)	0.569		
Genitourinary procedure	253 (1.2)	9 (0.9)	244 (1.2)	0.326		
No. (%) of patients with an initial urine culture by specimen type						
Clean catch/straight catheterized	18,252 (85.7)	933 (89.7)	17,319 (85.4)	Reference	Reference	
Indwelling catheterized	2,857 (13.4)	107 (10.3)	2,750 (13.6)	0.002	0.65 (0.53–0.80)	<0.001
Procedural[c]	197 (0.9)		197 (1.0)			
No. (%) of patients with an initial urine culture by location[d]						
ED and other outpatient facility[e]	907 (4.3)	175 (16.8)	732 (3.6)	<0.001	5.65 (4.70–6.78)	<0.001
Inpatient	20,399 (95.7)	865 (83.2)	19,534 (96.4)			
No. (%) of patients with an urinalysis[f]	6,738 (31.6)	310 (29.8)	6,428 (31.7)	0.196		
No. (%) of patients with an abnormal urinalysis[g]	3,915 (18.4)	170 (16.3)	3,745 (18.5)	0.080		
No. (%) of patients with the following discharge status[h]:						
Discharged to home	13,860 (65.5)	606 (58.9)	13,254 (65.9)	Reference	Reference	
Discharged to facility	5,419 (25.6)	284 (27.6)	5,135 (25.5)	0.010	1.10 (0.94–1.28)	0.086
Others[i]	1,879 (8.9)	139 (13.5)	1,740 (8.6)	<0.001	1.60 (1.31–1.95)	<0.001

[a]Includes inpatients who had single urine cultures or appropriate repeated urine cultures.
[b]This includes black (all patients = 5,447, patients with an inappropriate repeat urine culture = 251, remaining patients = 5,196) and other races (all patients = 1,210, patients with an inappropriate repeat urine culture = 60, remaining patients = 1,150).
[c]This included specimen collection by suprapubic aspiration, percutaneous nephrostomy tube placement, and cystoscopy.
[d]In the inappropriate repeat urine culture arm, 75% of the initial cultures were index cultures, while 25% were not.
[e]Outpatient facility (total = 82) included a clinic, skilled nursing facility, and long-term acute care facility.
[f]Urinalysis was performed either concomitantly with or within 1 h before the index urine culture.
[g]An abnormal urinalysis was defined as a leukocyte esterase value of ≥1 on urine dipstick and >5 white blood cells per high-power field on urine microscopy.
[h]There were 148 missing data.
[i]This included leaving against medical advice and death.
[j]Abbreviations: aOR, adjusted odd ratio; CI, confidence interval; IQR, interquartile range; CHF, congestive heart failure; ESRD, end-stage renal disease; HIV, human immunodeficiency virus; ED, emergency department.

than 48 h remained unclear, and the diagnostic yield of inappropriate repeat urine cultures was also not described in these two studies (2, 11).

The diagnostic gain from repeat clinical microbiology testing that is performed within a very short time frame is very limited (2, 3). Despite several clinical practice guidelines with recommendations for improving urine culturing practice (6, 12, 13), physician testing practices still vary (1, 2, 5, 11). Previous studies suggested potential factors contributing to unnecessary repeat testing, including an unawareness of pre-existing orders and a failure to determine when the last test was performed or to check

TABLE 2 Comparison of 1,120 pairs of index and inappropriate repeat urine cultures by ordering service[a]

Ordering service	No. (%) of samples with inappropriate repeat urine culture by ordering service[b]									
	General medicine	Surgery	ICU	SCT/oncology	Cardiology	Neurology/ neurosurgery	Gynecological oncology	Obstetrics	Orthopedics	Other inpatient locations[b]
Emergency department and other outpatient facilities[c] (n = 151)	47 (31.1)	30 (19.8)	48 (31.8)	16 (10.6)	5 (3.3)	3 (2.0)	1 (0.7)	0	1 (0.7)	0
General medicine (n = 133)	116 (87.2)	0	16 (12.0)	1 (0.8)	0	0	0	0	0	0
Surgery (n = 209)	0	190 (90.9)	17 (8.1)	1 (0.5)	0	0	1 (0.5)	0	0	0
ICU (n = 357)	9 (2.5)	8 (2.2)	332 (93.0)	0	3 (0.9)	5 (1.4)	0	0	0	0
SCT/oncology (n = 127)	0	0	12 (9.5)	115 (90.5)	0	0	0	0	0	0
Cardiology (n = 48)	0	0	10 (20.8)	0	38 (79.2)	0	0	0	0	0
Neurology/neurosurgery (n = 38)	2 (5.2)	0	11 (29.0)	0	0	25 (65.8)	0	0	0	0
Gynecologic oncology (n = 26)	0	1 (3.9)	0	0	0	0	25 (96.1)	0	0	0
Obstetrics (n = 6)	0	0	1 (16.7)	0	0	0	0	5 (83.3)	0	0
Orthopedics (n = 12)	0	0	0	1 (8.3)	0	0	0	0	11 (91.7)	0
Other inpatient locations[d] (n = 13)	2 (15.4)	0	3 (23.1)	0	0	0	0	0	0	8 (61.5)

[a]Abbreviations: ICU, intensive care unit; SCT, stem cell transplant.
[b]The shaded data are for samples for which repeat urine cultures were ordered by the same clinical service that ordered the index culture.
[c]Outpatient facilities included a clinic, skilled nursing facility, and long-term acute care facility.
[d]Included are observation and inpatient psychiatric units.

pending results (2, 3, 14, 15). In our current study, there was no significant difference in the proportion of associated urinalysis orders between the inappropriate repeat urine culture and the cultures for the control groups, suggesting a lack of awareness of the index culture results rather than the urinalysis results as the driving force for inappropriate repeat urine culturing practice. These factors could potentially explain our finding that most inappropriate repeat urine cultures were ordered by the same clinical service and that up to one-third were ordered by the same physician who ordered the index culture. ICUs had the highest number of inappropriate repeat urine cultures. We previously reported that isolated urine cultures, defined as urine cultures performed without additional diagnostic testing, such as urinalysis or urine microscopy, were more likely to be ordered among ICU patients (7). Interventions targeted to ICUs and physicians with outlying ordering behavior may therefore have a great impact on reducing inappropriate repeat testing.

Among the independent risk factors in our multivariable analysis, a more than 5-fold increased risk for having inappropriate inpatient repeat urine cultures performed within 48 h following the index culture was found when the initial urine culture was performed with a sample obtained in the emergency department. Other investigators have found similar findings for cardiac enzyme testing and suggested that unnecessary duplicative orders occurred more frequently when patients were transferred from the emergency department to inpatient units (16). The role of computerized physician order entry (CPOE) systems in altering physician ordering practices to reduce unnecessary laboratory testing has been well described (3, 8, 17). A computerized pop-up alert screen with pending results and the most recent completed test result with the date has resulted in a significant reduction in duplicate orders for ordering of panels of tests for acute hepatitis (17). A similar intervention to indicate to physicians that a recent urine culture was ordered, is pending, or has been completed, along with the time and date, may lead to more discerning utilization practices. A thoughtful design of CPOE systems coupled with the implementation of diagnostic stewardship may play an important role in improving the cost-effectiveness and quality of clinical patient care (18–20).

In this study, patients who had an index culture of a sample from an indwelling catheter had a lower risk of having an inappropriate repeat urine culture than those who had an index culture of clean-catch/straight catheterized and procedural specimens. This finding could potentially be explained by our institutional intervention of modifying urine testing order sets in the CPOE system, which was implemented in April 2016 (8). Urinalysis parameters of proteinuria and blood in the urine were excluded from reflex urine culture testing, with the exception of testing for neutropenic patients (8). This CPOE system-based intervention resulted in a significant reduction in the number of indwelling catheterized urine cultures (75.6%) being performed compared to the number of clean-catch urine cultures being performed (37.8%) (8). In our study, we assigned the indwelling catheterized urine cultures to preintervention (January 2015 to April 2016) and postintervention (May 2016 to February 2018) periods, based on our prior institutional intervention (8). We found that the proportion of all indwelling catheterized urine cultures was significantly lower during the postintervention period (3,217/16,308 [19.7%] versus 1,035/11,833 [8.7%]; $P < 0.001$). A similar finding was observed in the proportion of inappropriate repeat indwelling catheterized urine cultures in our cohort (219/760 [28.8%] versus 48/360 [13.3%]; $P < 0.001$).

A limitation of our study is that it is a retrospective study performed at a single, academic hospital, which limits the generalizability of our results to other settings. We did not include the data on antimicrobial use. The absence of chart review precluded the evaluation of test indication, provider characteristic (e.g., level of training), and longitudinal provider ordering behavior. To offset the lack of test indication by chart review, we used a relatively conservative definition for what constitutes an inappropriate repeat urine culture to avoid overestimating its prevalence. We also performed a sensitivity analysis and compared all inpatients who had repeat urine cultures performed within less than 48 h, irrespective of their clinical appropriateness criteria, and found similar results (data not shown). Although we used the Medicare Clinical

Laboratory Fee Schedule as a standardized method of reimbursement for urine culture, this may not reflect the actual laboratory costs, which may vary across hospitals. We were unable to assess the clinical consequences of reducing the number of inappropriate repeat urine cultures. However, previous studies postulated that elimination of unnecessary duplicative testing is unlikely to result in clinically significant adverse outcomes (2, 3, 11). The strengths of our study included a large sample size, a comparison of ordering services, an assessment of the transition of care from emergency department to inpatient services, and a measure of the potential financial impact of duplicate testing on laboratories.

In conclusion, we found in a large academic medical center that over half of urine cultures repeated on inpatients within 48 h were inappropriate. Notably, the diagnostic gain of an inappropriate repeat urine culture performed within 48 h for detecting bacteriuria was less than 5%. Further study is needed to evaluate provider-related ordering behavior on urine culturing practice and the effect of repeat urine culture testing on antimicrobial usage and clinical outcomes. Our findings highlight opportunities for further optimization of CPOE systems for improving diagnostic and antimicrobial stewardship and patient care.

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