

## RESEARCH BRIEF

## Clinical Significance of Low Colony-Count Urine Cultures Among Hospitalized Inpatients

Most hospital microbiology laboratories currently report uropathogen growth  $>10^4$  colony-forming units per milliliter (CFU/mL) from all voided or catheter urine cultures.<sup>1</sup> This threshold for reporting gained acceptance based on evidence suggesting that it confers improved sensitivity to detect acute cystitis in young female outpatients.<sup>2,3</sup>

The optimal threshold for reporting urine culture growth in hospitalized patients is not known. Before the threshold was lowered to improve sensitivity,  $>10^5$  CFU/mL was suggested as early as the 1950s, based on evidence that it detected  $>95\%$  of pyelonephritis cases.<sup>4</sup> Sixty years later, there is increased appreciation for the potential harms of over-detection of asymptomatic bacteriuria (ASB) among hospitalized patients in driving unnecessary antimicrobial therapy and the emergence of antimicrobial resistance.<sup>5,6</sup> We hypothesized that not routinely reporting urine cultures with colony counts  $10^4$ – $10^5$  CFU/mL among hospitalized patients, unless specially requested by a clinician, would result in a significant decrease in antimicrobial use for ASB with minimal risk of under-detecting urinary tract infection (UTI).

We performed a retrospective cohort study of all admitted patients with a low colony-count urine culture (ie,  $10^4$ – $10^5$  CFU/mL) collected on inpatient wards between March 1, 2016, and February 28, 2017, at our 627-bed acute-care hospital. Specimens from maternity units or operating rooms and those collected by cystoscopy or suprapubic aspiration were excluded. We compared the incidence of ASB, UTI, and bacteremia to a control cohort of inpatients with high colony-count urine cultures ( $>10^5$  CFU/mL) from the same units. Two investigators (M.A.S. and M.J.L.) performed retrospective chart reviews for all patients with consecutive low colony-count urine specimens and every fourth patient with a high colony-count urine specimen. UTI was defined as the presence of signs or symptoms, according to the National Healthcare Safety Network (NHSN) definition,<sup>7</sup> on the calendar day of urine culture collection (day 0) or the day preceding or following it ( $-1$  or  $+1$ ) in the absence of an alternate explanation. Interrater agreement was determined before completing full chart abstraction ( $\kappa$ , 0.8). New antimicrobial initiation was categorized in relation to the timing of urine culture collection (day 0), either as empirical (calendar days  $-1$  and 0) or reflexive (calendar days  $+1$  to  $+5$ ). Differences in proportions and medians were compared with a  $\chi^2$  and Mann-Whitney test, respectively. Our institutional research ethics board approved this study.

The characteristics of patients with low colony-count and high colony-count urine specimens are compared in Table 1.

Patient populations were similar in both groups (those with high colony count urine specimens were slightly older), but their microbiology and risk of infection differed significantly. High colony-count urine specimens comprised a larger proportion of *E. coli* and other *Enterobacteriaceae* specimens (59.7% vs 33.3%;  $P < .001$ ), while specimens with Enterococci and *Candida* spp were more highly represented among low colony-count specimens (45.4% vs 23.1%;  $P < .001$ ). Only 9.8% of low colony-count urine specimens were associated with UTI, compared with 17.2% of high colony-count specimens ( $P = .0009$ ). Bacteremic UTI occurred in 0.9% of low colony-count urine specimens compared with 2.1% of high colony-count specimens ( $P = .01$ ). After excluding patients with a high colony-count urine specimen collected within 24 hours of a low colony-count specimen, the proportion with a low colony-count UTI and bacteremic UTI decreased further to 7.8% and 0, respectively. When accounting only for Enterobacteriaceae, UTI was present in 13.8% of low colony-count urine specimens as opposed to 23.4% of high colony-count specimens ( $P = .06$ ). In terms of antimicrobial use generated by these urine specimens, few patients were initiated empirically on antimicrobial therapy for ASB regardless of colony count (6.5% vs 5.8%;  $P = .80$ ). Following urine culture

TABLE 1. Characteristics of Hospitalized Patients With Positive Urine Cultures With Low and High Colony Counts

Characteristic	Low Colony Count (n = 348), No. (%) <sup>a</sup>	High Colony Count (n = 186), No. (%) <sup>b</sup>	P Value
<b>Demographics</b>			
Median age, y (range)	69 (19–96)	74 (22–96)	<0.001
Female gender	187 (53.7)	112 (60.2)	0.15
Intensive care unit	89 (22.9)	36 (19.4)	0.33
Catheterized	107 (30.8)	63 (33.9)	0.45
<b>Microbiology</b>			
<i>E. coli</i>	74 (21.3)	71 (38.2)	
Other <i>Enterobacteriaceae</i>	42 (12.1)	40 (21.5)	
<i>Enterococcus</i> spp	90 (25.0)	29 (15.6)	
Yeast	68 (19.5)	14 (7.5)	
Other organisms or mixed	74 (21.3)	32 (17.6)	
<b>Clinical status</b>			
ASB	314 (90.2)	154 (82.2)	
UTI	34 <sup>c</sup> (9.8)	32 (17.2)	
Bacteremic UTI	3 <sup>d</sup> (0.86)	4 (2.1)	
<b>Antimicrobial use for ASB</b>			
Empirical, no alternate indication	14/216 (6.5)	7/121 (5.8)	
Reflexive, no alternate indication	77/216 (35.6)	60/121 (49.6)	

NOTE. ASB, asymptomatic bacteriuria; UTI, urinary tract infection; CFU, colony-forming units.

<sup>a</sup> $10^4$ – $10^5$  CFU/mL; units are no. (%) unless otherwise specified.

<sup>b</sup> $>10^5$  CFU/mL; units are no. (%) unless otherwise specified.

<sup>c</sup>7 patients also had a high colony-count urine specimen sampled within 24 h of the low colony-count urine collection.

<sup>d</sup>All 3 patients also had a high colony-count urine collected in preceding 24 h of the low colony-count urine collection.

reporting, reflexive therapy for ASB was initiated in 49.6% of high colony-count specimens versus 35.6% of low colony-count specimens ( $P = .01$ ).

Our results suggest that simply changing the threshold of reporting inpatient urine culture results could significantly reduce reflexive treatment of ASB with very low risk of underdetecting clinically significant urine cultures. The limited value of low colony-count urine specimens is not surprising given the high prevalence of bacteriuria among hospitalized patients compared to outpatients.<sup>6</sup> Our study externally validates the results of Kwon et al,<sup>8</sup> who identified as few as 4 of 48 UTIs (8.8%) among inpatient urines with  $10^4$ – $10^5$  CFU/mL.

Taken together, these findings call into question the benefits of routinely reporting  $10^4$ – $10^5$  CFU/mL growth from inpatient urine specimens. If our laboratory stopped routinely reporting these results unless specifically requested by a clinician with a high suspicion for a UTI, we could prevent up to 77 antimicrobial courses or 358 antibiotics days-of-therapy per year for ASB. The loss of sensitivity in detecting bacteriuria would translate into missing ~27 nonbacteremic UTI cases annually. If the laboratory could offer further processing of low count cultures upon clinician request, this could circumvent this concern with minimal extra work, estimated to be <30 phone requests per year.

Our study has several limitations. The retrospective design could overestimate ASB rates because of incomplete symptom documentation. However, the overall proportion (low colony count and high colony count combined) is similar to prospective evaluations in hospital settings.<sup>5</sup> The predicted impact of not reporting low colony-count urine specimens on antibiotic prescribing practices depends on clinician ability to request processing of these urine specimens only for patients with symptoms of UTI. This hypothesis requires confirmation in future intervention studies.

Low colony-count urine specimens are rarely associated with UTI and prompt significant unnecessary antimicrobial therapy. Changing the inpatient urine culture reporting threshold should be considered for future laboratory-driven antimicrobial stewardship interventions to reduce treatment of ASB.

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Marc-André Smith, MD, MSc;<sup>1,2</sup>  
 Michael J. Lamb, MD;<sup>4</sup>  
 Laura Baillie, BSc, ART;<sup>2</sup>  
 Andrew Simor, MD;<sup>2,3,4</sup>  
 Jerome A. Leis, MD, MSc<sup>1,3,4</sup>

Affiliations: 1. Center for Quality Improvement and Patient Safety, University of Toronto, Toronto, Ontario, Canada; 2. Department of Microbiology, Sunnybrook Health Sciences Center, Toronto, Ontario, Canada; 3. Division of Infectious Diseases, Sunnybrook Health Sciences Center, Toronto, Ontario, Canada; 4. Department of Medicine, University of Toronto, Toronto, Ontario, Canada.

Address correspondence to Marc-André Smith, MD, MSc, Sunnybrook Health Sciences Centre, 2075 Bayview Avenue, Toronto, Ontario M4N 3M5 (marc-andre.smith.cnmtl@ssss.gouv.qc.ca).

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