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Epidemiology of Hospital-Acquired Urinary Tract-Related Bloodstream Infection at a University Hospital

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Abstract

Little is known about the epidemiology of nosocomial urinary tract-related bloodstream infection. In a case series from an academic medical center, *Enterococcus sp.* (28.7%) and *Candida sp.* (19.6%) were the predominant microorganisms isolated, suggesting a potential shift from previously observed Gram-negative microorganisms. A case-fatality rate of 32.8% highlights the severity of this condition.

Urinary tract infection (UTI) is the most frequent healthcare-associated infection in the United States. Bloodstream infection secondary to nosocomial bacteriuria occurs less frequently, but is associated with substantial morbidity and mortality,[1] heightening the desire to prevent this healthcare-associated infection. Despite renewed interest in nosocomial UTIs, in part due to the recent decision by the Centers for Medicare and Medicaid Services to no longer reimburse hospitals for UTIs not present on admission,[2] surprisingly little is known about the epidemiology of nosocomial urinary tract-related bloodstream infection. We conducted the following study to describe the epidemiologic features of patients with this nosocomial infection.

Methods

We conducted a retrospective review of nosocomial urinary tract-related bloodstream infections from 2000 to 2008 at the University of Michigan Health System. Cases were defined as any adult (≥21 years of age) meeting all of the following criteria: (a) positive urine and blood culture with the same microorganism during their hospital stay; (b) positive urine culture obtained prior to, or on the same day as, positive blood culture; (c) positive urine culture not obtained within the first 2 days of admission; and (d) positive blood culture obtained within 14 days of positive urine culture. A urine culture was defined as positive if >

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10^3 CFU/ml of a single organism grew.[3] Manual record review for all cases was performed by an infectious diseases physician (E.S.) to exclude cases with primary bloodstream infection with hematogenous spread to the kidney.

Administrative data and medical records were used to obtain demographic, clinical, microbiological, and additional information during the hospitalization. Coexisting conditions were defined by the presence of ICD-9-CM codes. Neutropenia was defined by laboratory values (neutrophil count ≤ 500 cells/MM^3). Descriptive statistics were used to characterize the population. Chi-square tests of association were used to assess bivariate comparisons. Alpha was set at 0.05, 2-tailed. Analyses were conducted using Stata/SE 11 (College Station, TX).

Results

Of the 355 patients meeting the case definition, 35 patients (9.9%) were excluded due to primary bloodstream infection, leaving 320 patients in our study.

Table 1 displays the select patient characteristics. A slight male predominance was observed (55.3%). Patients were hospitalized for a median of 30.0 days (range 4–251 days). A total of 33.4% of the patients were discharged home, 32.8% died, 29.7% transferred to an intermediate level of care for further recovery, and 4.1% went to hospice. Renal disease (51.9%), malignancy (40.9%), diabetes mellitus (23.1%), and neutropenia (21.6%) were the most frequent conditions observed.

The distribution of the microorganisms isolated and genus-specific case-fatality rates are presented in Table 2. Gram-negative infections affected approximately one-third of our patient population. Throughout the study period, infections were most frequently due to *Enterococcus sp.* and *Candida sp.*, accounting for nearly half of all infections. Vancomycin-resistant enterococcus (VRE) isolates were more common than vancomycin-sensitive enterococcus (VSE), accounting for 16.2% and 12.2% of infections respectively. *Enterococcus sp*. were more frequent in patients with a history of neutropenia (p=0.002), renal disease (p=0.024), or transplantation (p=0.010). *Candida sp.* were more frequent in patients with a history of liver disease (p=0.001) or renal disease (p=0.004), and less frequent in patients with transplantation (p=0.029).

The overall case-fatality rate observed in this case series was 32.8% (95% CI: 27.7%–38.2%). Patients with *Candida sp.* had the highest case-fatality rate (49.2%; 95% CI: 36.4%–62.1%). Compared to patients with *E. coli* infections, patients with *Candida sp.* infections had a 3.4 times greater risk of mortality (95% CI: 1.5–7.3). The case-fatality rate was significantly higher in patients with VRE than with VSE (42.3% and 17.9%, respectively); individuals with VRE were 2.4 times more likely to die during hospitalization than patients with VSE (RR=2.4; 95% CI: 1.2–5.1).

Discussion

In our case series of patients with nosocomial urinary tract-related bloodstream infection, we observed a predominance of *Enterococcus sp.* or *Candida sp.* infections. Overall, clinical outcomes were generally poor, with one-third of patients requiring placement in another facility, one-third dying before discharge, and only ~10% patients returning home without any form of assistance.

Few studies have evaluated the epidemiology of patients who develop nosocomial bloodstream infection from a urinary source. Age, urethral catheters, urologic disease, male sex, malignancy, diabetes, smoking, and immunosuppressant therapy have been previously

identified as potential risk factors for developing urinary tract-related bloodstream infection.[4,5,6] Gram-negative microorganisms have been found to be the predominant agents of bloodstream infection arising from UTIs.[4,5,6] Previous studies have shown the infection rates due to *Enterococcus sp.* and *Candida sp.* to be < 16% and < 10%, respectively,[4,5,6,7] while these microorganisms accounted for nearly 29% and 20% of the infections in our case series.

Among the few studies investigating urinary tract-related bloodstream infection, case-fatality rates have ranged from 7.5%[4] to 16.2%.[8] Comparatively, one-third of the patients died during hospitalization in our case series. High rates of comorbid conditions, extensive length of stay, an increased *Candida sp.* infection rate with attendant mortality as well as high rates of VRE (which is not typically covered in empiric antimicrobial regimens) are all factors that likely contribute to this finding.

Our study has several limitations. First, this study was performed without controls, limiting our ability to draw causal inferences. Infections with *Enterococcus sp.* or *Candida sp.* could be markers for severity of illness in these complex patients. Second, the retrospective nature of our study affected our ability to determine whether UTIs reflect a primary urinary infectious nidus or seeding from a hematogenous site. We addressed this, however, by eliminating cases believed to have a clear competing bloodstream infectious source. Third, we did not directly exclude patients who had cultures of the same organism from an alternative location. Fourth, we did not examine the adequacy of antimicrobial therapies, or compare resistance patterns to antimicrobials between urine and blood isolates. Fifth, this was a single-site study performed in a Midwestern referral hospital that cares for complex patients, and the generalizability of our findings may be limited. Finally, we were unable to consistently determine certain variables through administrative or clinical records (e.g., the presence of indwelling urethral catheter).

Despite these limitations, our case series contributes to the limited body of literature and demonstrates a potential change in the epidemiology of nosocomial urinary tract-related bloodstream infection from predominantly Gram-negative bacteria to predominantly *Enterococcus sp.* and *Candida sp.* One alternative explanation for this finding is the elimination of typical gram-negative infections by traditional antibiotic coverage that most high-risk hospitalized patients (e.g., neutropenic or transplanted patients) receive, resulting in the appearance of an epidemiologic shift. A second alternative would be selective pressure from broad-spectrum antimicrobials resulting in colonization with VRE[9] and a predisposition to *Candida sp.* infections. Given our inability to discriminate between these alternatives, these preliminary findings should not be used to motivate changes in current practice.

Importantly, our results suggest that as many as two-thirds of patients with nosocomial urinary tract-related bloodstream infection may either be transferred to long-term care facilities upon hospital discharge or die during hospitalization. Efforts to prevent nosocomial UTI and subsequent bloodstream infection continue to be needed.

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Table 1

Characteristics of 320 Patients with Hospital-Acquired Urinary Tract-Related Bloodstream Infection, 2000–2008

Characteristic	Total n=320
Age, mean (range)	58.1 (21–92)
Age, mean (range) – expired	56.9 (21–88)
Age, mean (range) – survived	58.7 (21–92)
Gender	
Male	177 (55.3%)
Female	143 (44.7%)
Race	
Caucasian	257 (80.3%)
African American	35 (10.9%)
Unknown/Other	28 (8.8%)
Length of Stay - days	
Mean	40.6
Median	30.0
Range	4–251
Admitting Source	
Emergency department	122 (38.1%)
Home	81 (25.3%)
Clinic admit (n=41)	
Admit from home (n=39)	
From observation (n=1)	
Transfer from another acute-care hospital	54 (16.9%)
From outpatient procedure/day of procedure	51 (15.9%)
Other/Unknown[+]	12 (3.8%)
Insurance	
Commercial	158 (49.4%)
Medicare	134 (41.9%)
Medicaid	21 (6.6%)
Other	7 (2.2%)
Discharge Disposition	
Home	107 (33.4%)
Home – order for home health service (n=75)	
Home – self-care (n=32)	
Expired	105 (32.8%)
Transfer	95 (29.7%)
Transfer – skilled nursing facility (n=44)	
Transfer – other facility (n=6)	
Transfer – short term acute facility (n=12)	

Characteristic	Total n=320
Transfer – another rehab facility (n=25)	
Transfer – long term care facility (n=8)	
Hospice	13 (4.1%)
Profile of co-morbidities* (All diagnoses, primary or secondary)	
Surgery	268 (84.1%)
Renal Failure and/or Renal Disease	166 (51.9%)
Malignancy	131 (40.9%)
Diabetes	74 (23.1%)
Neutropenia	69 (21.6%)
Transplant	67 (20.9%)
Liver Disease	57 (17.8%)
Benign Prostatic Hypertrophy	11 (3.4%)

†Includes Transfer from other facility, DPU=distinct part unit (rehab unit/psych unit) (separate admission), transfer from correctional facility and unknown/missing

*Defined using a two-step process: 1) by the presence/absence of any of the ICD-9 codes used to categorize each Elixhauser category and 2) additional ICD-9 codes as selected by the investigator team. Categories are according to comorbidity software version 3.3 found on the Healthcare Cost and Utilization Project (HCUP) website: http://www.hcup-us.ahrq.gov/toolssoftware/comorbidity/comorbidity.jsp#download.

Neutropenia as defined by laboratory values (neutrophil count ≤ 500).

Transplant as defined by the presence of ICD9 codes 996.0, 996.8, E878.0, V42.0, V42.1, V42.2, V42.7, V42.81, V42.82 and V42.83.

BPH as defined the presence of ICD-9 codes 600–600.9.

Table 2

Distribution of Microorganisms among Patients with Hospital-Acquired Urinary Tract-Related Bloodstream Infection, 2000–2008

Microorganism (genus):	All Patients (n=320)	Genus-specific Case-fatality
Enterococcus sp.	91 (28.4%)	29 (31.9%)
Vancomycin-resistant	52 (16.2%)	22 (42.3%)
Vancomycin-sensitive	39 (12.2%)	7 (17.9%)
Candida sp.	63 (19.7%)	31 (49.2%)
Escherichia coli	41 (12.8%)	6 (14.6%)
Coagulase-positive staphylococcus	28 (8.8%)	12 (42.9%)
Pseudomonas sp.	26 (8.1%)	9 (34.6%)
Coagulase-negative staphylococcus	19 (5.9%)	4 (21.1%)
Klebsiella sp.	18 (5.6%)	6 (33.3%)
Enterobacter sp.	14 (4.4%)	4 (28.6%)
Proteus sp.	5 (1.6%)	1 (20.0%)
Acinetobacter sp.	4 (1.2%)	1 (25.0%)
Citrobacter sp.	4 (1.2%)	1 (25.0%)
Other	4 (1.2%)	1 (25.0%)
Streptococcus sp.	3 (0.9%)	0 (0.0%)

Other microorganism category includes Elizabethkingae, Morganella, and Serratia microorganisms