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Major Article

The epidemiology of hospital-acquired urinary tract-related bloodstream infection in veterans

Payal K. Patel MD, MPH [a,b,c,*], M. Todd Greene PhD, MPH [c,d,e], Mary A.M. Rogers PhD [c,d,e], David Ratz MS [c,d], Latoya Kuhn MPH [c,d], Jennifer Davis MHSA [d], Sanjay Saint MD, MPH [c,d,e]

[a] *Division of Infectious Diseases, VA Ann Arbor Healthcare System, Ann Arbor, MI*
[b] *Division of Infectious Diseases, University of Michigan Health System, Ann Arbor, MI*
[c] *Department of Veterans Affairs, University of Michigan Patient Safety Enhancement Program, Department of Veterans Affairs Hospital, Ann Arbor, MI*
[d] *Center for Clinical Management Research, VA Ann Arbor Healthcare System, Ann Arbor, MI*
[e] *Division of General Medicine, University of Michigan Health System, Ann Arbor, MI*

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Background: Hospital-acquired urinary tract-related bloodstream infections are rare but often lethal. Recent epidemiology of this condition among the United States veteran population is poorly described.
Methods: We conducted a retrospective review of hospital-acquired urinary tract-related bloodstream infections of adult inpatients admitted to 4 Veterans Affairs hospitals over 15 years. Electronic medical records were used to obtain clinical, demographic, and microbiologic information. Descriptive statistical analyses were conducted using chi-square tests of association. Test for trend was performed by genus of organism and for case fatality rate over time.
Results: While the most commonly isolated organisms were *Staphylococcus* spp. (36.5%), the incidence of infections caused by *Escherichia* and *Klebsiella* increased over time ($P = .02$ and $P = .03$, respectively). The overall in-hospital case fatality rate was 24.2% in 499 patients. The case fatality rate was 25.8% for patients with *Staphylococcus* infections and 20.7% for patients with enterococcal infections.
Conclusions: Hospital-acquired urinary tract-related bloodstream infection is commonly due to *Staphylococcus* spp. and is related to the high fatality among United States veterans. Focused infection control efforts could decrease the incidence of this fatal infection.

Urinary tract-related bloodstream infections acquired during hospitalization can cause substantial morbidity and mortality. Previous studies have reported that up to 3% of patients in acute care facilities with hospital-acquired bacteriuria develop a related bloodstream infection.[1] Veterans are especially susceptible to this complication given that they are predominantly male, and men have been found to develop secondary bloodstream infections due to hospital-acquired urinary tract infection twice as often as women, which is thought to be reflective of structural genitourinary tract abnormalities in this population.[2] Additional risk factors previously identified for this infection include age, presence of urethral catheter, urologic disease, malignancy, diabetes mellitus, neutropenia, renal disease, smoking, and immunosuppressant therapy.[3-5] Compared to the general population, Veterans Affairs (VA) patients tend to have a prevalence higher than the general population of some of these risk factors—such as diabetes mellitus and presence of a urinary catheter—and are an ideal group in which to study this disease state.[3,6]

National quality measures have increasingly focused on healthcare-associated infections; therefore, learning more about the etiology of hospital-acquired urinary tract-related bloodstream infections may help inform preventive interventions.[7,8] Previous studies have described the epidemiology of urinary tract-related bloodstream infections,[2,5,9,10] but most have been limited to single sites. A previous single-site study identified risk factors for urinary tract-related bloodstream infections among a veteran population; however, these patients were hospitalized between 1984 and 1999.[4] As such, we investigated urinary tract-related bloodstream infection within the veteran population at 4 diverse VA hospitals, 1 in the South and 3 in the Midwest, to examine whether the microbiology of urinary tract-related bloodstream infection is evolving and to assess the case fatality rate due to this infection.

* Address correspondence to Payal K. Patel, MD, MPH, Division of Infectious Diseases, Department of Internal Medicine, University of Michigan Medical School, Veterans Affairs Ann Arbor Healthcare System, 2215 Fuller Rd, Ann Arbor, MI 48105.
E-mail address: payalkp@umich.edu (P.K. Patel).
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METHODS

We conducted a retrospective review of hospital-acquired urinary tract-related bloodstream infections among adult veteran inpatients admitted to four VA hospitals over 15 years (January 1, 2000, to December 31, 2014). Cases were defined as patients with urine and blood cultures that grew the same organism with the following criteria: urine culture obtained 48 hours or more after admission, urine culture obtained prior to or the same day as the blood culture, and positive blood culture within 14 days of positive urine culture. The urine culture was considered positive if more than 10^3 CFU/ml of a single organism grew.[11] Electronic medical records were used to obtain clinical, demographic and microbiologic information. Manual medical record reviews of all cases were conducted by a research nurse to exclude cases with primary bloodstream infection with hematogenous spread to the kidney. Descriptive statistical analyses were conducted using t-tests and chi-square tests of association, and a test for trend was performed by genus and for case fatality rates over time. Analyses were performed using SAS version 9.4 software (Cary, NC). The study received human subjects institutional review board approval from the VA Ann Arbor Healthcare System.

RESULTS

A total of 499 patients met the case selection criteria. Patient characteristics are displayed in Table 1. The mean age was 67.2 years, the median age was 67 years, and most patients were white (56.3%). Patients who survived were younger on average than those who died (65.9 years vs. 71.0 years, $P < .0001$). The study population was mostly male (98.6%), as expected for a VA population. The median length of stay was 26 days, and the mean time from admission to bloodstream infection was 19.85 days. Upon discharge, 58.3% of patients were discharged home, 24.2% died in the hospital and 16.0% were transferred to another facility, VA or community nursing home. Surgery during the concurrent admission was noted in 59.3% of patients. Diabetes mellitus (27.5%), neutropenia (22.2%), malignancy (20.4%), and renal disease (18.6%) were the most prevalent comorbidities. Of patients with urinary tract-related bloodstream infections, 42.1% had an indwelling urethral catheter on the date that they had a positive blood culture that met case criteria, and 64.9% of patients had a urethral catheter at some time between admission and the time they were found to have a positive blood culture that met case criteria for a urinary tract-related bloodstream infection.

Table 1
Baseline characteristics of 499 patients with hospital-acquired urinary tract-related bloodstream infections

Characteristic	Total (n = 499)
Age in years, mean (range)	67.2 (24-95)
Age in years, mean (range)—died	71.0 (46-95)
Age in years, mean (range)—survived	65.9 (24-92)
Sex	
Men	492 (98.6%)
Women	7 (1.4%)
Race	
White	281 (56.3%)
Black	175 (35.1%)
Other/Declined/Missing	43 (4.6%)
Length of Stay (days)	
Mean	46.8
Median	26
Range	4-1440
Discharge Disposition	
Home	291 (58.3%)
Died	121 (24.2%)
Transfer to nursing home	69 (13.8%)
Transferred to other VA hospital	11 (2.2%)
Irregular discharge	7 (1.4%)
Conditions*	
Surgery at current admission	296 (59.3%)
History of renal failure or renal disease	93 (18.6%)
History of malignancy	102 (20.4%)
Diabetes mellitus	137 (27.5%)
Neutropenia	111 (22.2%)
History of transplant	2 (0.4%)
Liver disease	43 (8.6%)
Benign prostatic hypertrophy	31 (6.2%)
Urinary catheter presence	
At time of infection	210 (42.1%)
Any time after admission	324 (64.9%)

*Patients were coded for multiple conditions if these coexisted.

Gram-negative bacterial organisms were involved in the infections of more than half (56.7%) of all cases. Very few isolates (1.6%) were found to have an extended-spectrum β-lactamase (ESBL)-producing organism. *Staphylococcus* was the most common genus associated with infection (36.5%), with coagulase-negative *Staphylococcus* being the most common species. Conventional genitourinary organisms were frequently found: *Escherichia coli* was the second most common cause of infection (19.2%), and *Klebsiella* spp. was found in 8.4% of infections. Only 10.2% of infections were caused by *Candida* species. Of these, the predominant organism was *Candida albicans*.

Overall, the case fatality rate was 24.2%. Adjusting for age, malignancy, and diabetes, having a surgery during the stay was associated with increased in-hospital mortality (relative risk = 1.61, $P = .01$). A total of 25.8% of patients with a *Staphylococcus* infection and 20.7% with an enterococcal infection died in the hospital. Although *Pseudomonas* and *Enterobacter* infections were less common (9.0% and 3.0%, respectively), both were associated with a 20.0% case fatality rate. Genus-specific time trends in infection are presented in Figure 1. Overall, *Staphylococcus* infections decreased over time ($P = .11$), whereas disease due to conventional genitourinary organisms, *E. coli* and *Klebsiella* spp., increased ($P = .02$ and $P = .03$, respectively).

DISCUSSION

We investigated the epidemiology of hospital-acquired urinary tract-related bloodstream infections at four VA hospitals over a 15-year period. Several important findings on the microbiology and mortality associated with this infection emerged from our study. First, we showed a potential shift in the distribution of organisms related to urinary tract-related bloodstream infections acquired during hospitalization. While *Staphylococcus* spp. remain common organisms, gram-negative organisms caused the most infections, a finding which differed from some previous studies.[2,9,10] Second, few multidrug-resistant gram-negative organisms were seen; and *Candida albicans*, which is not commonly associated with antifungal drug resistance,[12] was the most prevalent fungal organism, which is reassuring from an antimicrobial resistance perspective. Third, we identified a high case fatality rate among patients with hospital-acquired urinary tract-related bloodstream infections (Table 2).

Previous studies that investigated the microbiology of urinary tract-related bloodstream infections have largely been single-center studies. These studies found that the associated mortality of this infection is high; that gram-negative bacteria (such as *E. coli*) tend to be the primary etiologies of urinary tract-related bloodstream infections; and that risk factors include genitourinary pathology, presence of urinary catheter, age, male sex, history of diabetes mellitus, malignancy, and recent surgery.[2,3,9] In a study conducted at a single-site, academic, non-VA hospital, Chang et al.