RESEARCH LETTER

Bloodstream Infections in Hospitalized Hemodialysis Patients

To the Editor:

Bloodstream infections (BSIs) are the most common infections among maintenance hemodialysis patients and are associated with considerable morbidity and mortality.[1] From 2003 to 2012, rates of BSI and sepsis hospitalizations in this patient population increased by 40%.[2] There is a paucity of recent data pertaining to causative pathogens and antimicrobial resistance rates causing BSIs.

From January 1, 2009, to December 31, 2017, a retrospective study was conducted to quantify the trends in pathogens and their antimicrobial-resistant profiles causing BSIs among maintenance hemodialysis patients admitted to a 700-bed and a 255-bed tertiary-care hospital in Providence, RI. Approval from the ethics board was obtained (institutional review board 1158504-5). Due to the use of deidentified patient data, the need for informed consent was waived.

BSIs were identified using Theradoc (Premier, Inc). This clinical surveillance software is used nationwide by infection preventionists to monitor infections within hospitals. Requirement for maintenance hemodialysis was obtained through Theradoc and confirmed by review of electronic medical records. Data for type of hemodialysis access or source of BSI were not available from Theradoc. All positive blood cultures were considered true BSIs, except for coagulase-negative *Staphylococcus* spp, which required review of the patient's electronic medical record and documentation of directed treatment by the provider. BSIs were considered hospital acquired if the first positive blood culture was collected 48 hours or longer after admission. Multiple positive blood cultures for the same pathogen identified in a patient during the same admission were counted as a single BSI.

Antimicrobial susceptibility profiles were obtained from the electronic medical record's microbiology reports. Clinical and Laboratory Standards Institute's standards for antimicrobial susceptibility testing were used.[3] Isolates with intermediate resistance to a specific antimicrobial were classified as resistant. Data were analyzed using SAS, version 9.4 (SAS Institute). Cochran-Armitage test for linear trends was used to examine trends in causative pathogens and antimicrobial resistance.

During the study period, a total of 542 BSIs, caused by 559 isolates, were identified among 521 hospitalized maintenance hemodialysis patients. Seventeen (3.1%) BSIs were polymicrobial and 89 (16.4%) were hospital-acquired infections. Pathogen distribution by type is shown in Table 1. Gram-negative bacterial species were *Escherichia coli* (34.2% of total gram-negative bacteria), *Klebsiella* spp (20.8%), *Pseudomonas aeruginosa* (10.7%), *Enterobacter* spp (10.7%), *Serratia* spp (6.7%), *Acinetobacter* spp (4.7%), *Stenotrophomonas* spp (3.4%), *Proteus* spp (3.4%), *Citrobacter* spp (2.7%), *Morganella morganii* (1.3%), *Salmonella* spp (0.7%), and *Haemophilus* spp (0.7%).

There was a statistically significant increase in gram-negative pathogens and decrease in *S aureus* causing BSIs during the 9-year study period ($P = 0.003$ and $P = 0.002$, respectively). There were no statistically significant changes in trends during the study period for specific gram-negative species ($P > 0.05$). The percent of pathogens resistant to specific antimicrobial or antimicrobial classes per study year is shown in Table 2.

In this 9-year hospital-based study, gram-negative bacteria were the second most common pathogens causing BSIs, after *S aureus*. Rates of BSI caused by gram-negative bacteria increased during the study period, whereas rates of BSI caused by *S aureus* decreased. In 2017, the last year of the study, BSIs caused by gram-negative bacteria were more common than those

Table 1. Distribution of Pathogens Associated With Bloodstream Infections Among Hospitalized Maintenance Hemodialysis Patients

Pathogen	Total Isolates	No. (% of all pathogens)									*P*
		2009	2010	2011	2012	2013	2014	2015	2016	2017	
Staphylococcus aureus	252 (45.1%)	29 (48.3%)	37 (43.0%)	49 (55.1%)	32 (54.2%)	30 (65.2%)	17 (29.3%)	24 (60.0%)	21 (29.6%)	13 (26.0%)	0.002
Gram-negative bacteria	149 (26.7%)	15 (25.0%)	19 (22.1%)	15 (16.9%)	14 (23.7%)	9 (19.6%)	24 (41.4%)	9 (22.5%)	25 (35.2%)	19 (38.0%)	0.003
Coagulase-negative *Staphylococcus* spp	66 (11.8%)	6 (10.0%)	19 (22.1%)	12 (13.5%)	3 (5.1%)	2 (4.3%)	5 (8.6%)	0 (0.0%)	11 (15.5%)	8 (16.0%)	0.5
Enterococcus spp	46 (8.2%)	8 (13.3%)	3 (3.5%)	10 (11.2%)	1 (1.7%)	2 (4.4%)	7 (12.1%)	3 (7.5%)	7 (9.9%)	5 (10.0%)	0.7
Streptococcus spp	30 (5.4%)	1 (1.7%)	3 (3.5%)	1 (1.1%)	8 (13.6%)	2 (4.4%)	4 (6.9%)	4 (10.0%)	3 (10.0%)	4 (8.0%)	0.08
Fungi[a]	16 (2.9%)	1 (1.7%)	5 (5.8%)	2 (2.3%)	1 (1.7%)	1 (2.2%)	1 (1.7%)	0 (0.0%)	4 (5.7%)	1 (2.0%)	0.9
Total	559 (100%)	60 (100%)	86 (100%)	89 (100%)	59 (100%)	46 (100%)	58 (100%)	40 (100%)	71 (100%)	50 (100%)	0.2

[a]All were identified as *Candida* spp, except for 1 *Cryptococcus* sp in 2016.

Table 2. Number and Percent of Pathogens That Tested Resistant to Selected Antimicrobials, Per Year of Study

	No. of Resistant Isolates/No. of Isolates Tested (%)									
Pathogen, Antimicrobial	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	***P***
Staphylococcus aureus										
Methicillin	16/29 (55.2%)	19/37 (51.4%)	29/49 (59.2%)	11/32 (34.4%)	16/30 (53.3%)	6/17 (35.3%)	8/24 (33.3%)	11/21 (52.4%)	5/13 (38.5%)	0.1
Enterococcus spp										
Vancomycin	4/8 (50.0%)	2/3 (66.6%)	3/10 (30.0%)	0/1 (0.0%)	1/2 (50.0%)	3/7 (42.9%)	0/3 (0.0%)	1/7 (14.3%)	2/5 (40%)	0.2
Gram-negative bacteria										
Aminoglycosides[a]	0/15 (0.0%)	0/17 (0.0%)	3/15 (20.0%)	6/14 (42.9%)	1/9 (11.1%)	4/23 (17.4%)	0/9 (0.0%)	3/22 (13.6%)	3/17 (17.6%)	0.4
Extended-spectrum cephalosporins[b]	5/14 (35.7%)	3/18 (16.7%)	2/15 (13.3%)	3/14 (21.4%)	1/9 (11.1%)	2/22 (9.1%)	2/9 (22.2%)	6/25 (24.0%)	7/18 (38.9%)	0.5
Meropenem	0/15 (0.0%)	1/17 (5.9%)	0/15 (0.0%)	0/14 (0.0%)	0/9 (0.0%)	1/22 (4.5%)	0/9 (0.0%)	0/22 (0.0%)	1/17 (5.9%)	0.7
Piperacillin/tazobactam	2/14 (14.3%)	3/18 (16.7%)	0/13 (0.0%)	3/13 (23.0%)	0/9 (0.0%)	3/21 (14.3%)	1/8 (12.5%)	1/25 (4.0%)	2/18 (11.1%)	0.4
Fluoroquinolones[c]	3/15 (20.0%)	1/18 (5.5%)	3/15 (20.0%)	8/14 (57.1%)	1/9 (11.1%)	5/23 (21.7%)	1/9 (11.1%)	5/25 (20.0%)	3/19 (15.8%)	0.9
Multidrug resistant[d]	2/14 (14.3%)	0/17 (0.0%)	0/17 (0.0%)	3/13 (23.1%)	0/9 (0.0%)	1/21 (4.8%)	0/8 (0.0%)	2/22 (9.1%)	2/17 (11.8%)	0.7

[a]Tobramycin and/or gentamicin.
[b]Cefepime, ceftazidime, and ceftriaxone.
[c]Ciprofloxacin and levofloxacin.
[d]Resistance to at least 1 antimicrobial in 3 or more antimicrobial categories, which included extended-spectrum cephalosporins, fluoroquinolones, aminoglycosides, meropenem (all organisms); and piperacillin/tazobactam (Enterobacteriaceae and *Pseudomonas aeruginosa*). Denominators represent number of isolates tested to all antimicrobials/classes.

caused by *S aureus* (38.0% and 26.0%, respectively). Future studies need to verify the findings of this 2-center study.

The increase in gram-negative pathogens implicated in BSIs among maintenance hemodialysis patients is of great concern because they are commonly associated with severe sepsis and mortality rates of up to 38%.[4,5] Studies have shown that antimicrobial resistance among gram-negative bacteria is also of great concern because rates are rapidly increasing.[6] Resistance to multiple antimicrobials is also frequent and severely limits therapeutic options. For example, infections caused by carbapenemase-producing gram-negative bacteria are resistant to carbapenems, cephalosporins, and many other antimicrobials, leaving polymyxins such as colistin as the only remaining effective antimicrobial.[7]

In the last year of this study, resistance to extended-spectrum cephalosporins, such as cefepime, reached 38.9% among gram-negative bacteria. These antimicrobials are frequently used as empiric treatment for presumed BSIs and therefore these high percentages warrant concern. Furthermore, 11.8% of gram-negative bacteria were resistant to 3 or more antimicrobial classes, including extended-spectrum cephalosporins, fluoroquinolones, and carbapenems. Although an increase in resistance rates was not detected, this is likely due to a small sample size because it is well established that rates are increasing in other patient populations.[7]

Overuse of antimicrobials is one of the main mechanisms for the emergence and spread of antimicrobial-resistant pathogens. Antimicrobial stewardship programs implemented in dialysis facilities have shown substantial reduction in unnecessary antimicrobial prescribing and should be implemented in all facilities.[8] Cross-transmission between patients is another main mechanism of spread and preventive efforts in dialysis facilities predominantly focus on methicillin-resistant *S aureus* and vancomycin-resistant enterococci.[9] The results of this study suggest that consideration to expand to antimicrobial-resistant gram-negative pathogens may be warranted.

Larger scale studies, such as those conducted by the National Healthcare Safety Network, are needed to fully understand the evolving epidemiology of BSIs among maintenance hemodialysis patients.[1]

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