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Abstract

This cross-sectional study at a tertiary-care hospital in Botswana from 2000 to 2007 was performed to determine the epidemiologic characteristics of *Staphylococcus aureus* bacteremia. We identified a high prevalence (11.2% of bacteremia cases) of methicillin-resistant *S. aureus* (MRSA) bacteremia. MRSA isolates had higher proportions of resistance to commonly used antimicrobials than did methicillin-susceptible isolates, emphasizing the need to revise empiric prescribing practices in Botswana.

Keywords

Staphylococcus aureus bacteremia, Botswana, HIV, children

Disciplines

Diseases | Medicine and Health Sciences | Virus Diseases

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CONCISE COMMUNICATION

Epidemiology of Methicillin-Resistant *Staphylococcus aureus* Bacteremia in Gaborone, Botswana

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This cross-sectional study at a tertiary-care hospital in Botswana from 2000 to 2007 was performed to determine the epidemiologic characteristics of *Staphylococcus aureus* bacteremia. We identified a high prevalence (11.2% of bacteremia cases) of methicillin-resistant *S. aureus* (MRSA) bacteremia. MRSA isolates had higher proportions of resistance to commonly used antimicrobials than did methicillin-susceptible isolates, emphasizing the need to revise empiric prescribing practices in Botswana.

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In sub-Saharan Africa, *Staphylococcus aureus* is a common cause of bacteremia.¹⁻⁵ High regional prevalence rates of the human immunodeficiency virus (HIV) may contribute to increased incidence and mortality rates of *S. aureus* bacteremia. To our knowledge, the epidemiologic characteristics of *S. aureus* bacteremia in Botswana are unknown.

Knowledge of the epidemiologic characteristics of *S. aureus* bloodstream isolates influences treatment decisions and has broad public health implications.⁶ Construction of empiric prescribing guidelines based on local susceptibility profiles may improve care delivery, optimize available resources, and decrease mortality.

Our primary objective was to determine the epidemiologic characteristics of *S. aureus* bacteremia in hospitalized adults and children in Gaborone, Botswana, over an 8-year period. Secondary objectives were to identify patient characteristics associated with methicillin-resistant *S. aureus* (MRSA) and to determine antimicrobial susceptibilities of *S. aureus* isolates.

METHODS

This cross-sectional study was performed at Princess Marina Hospital, a 530-bed hospital in Gaborone, Botswana, with approximately 25,000 annual admissions. The prevalence of HIV in Botswana's adult population is estimated at 17% and reaches 30%–40% among adults aged 25–44 years. The prevalence among children 1.5–4 years of age is 6.3%.⁷ The inpatient population of Princess Marina Hospital reflects the high regional HIV prevalence. Highly active antiretroviral therapy has been available free of charge since 2002. This study received approval from the institutional review boards

of the Children's Hospital of Philadelphia and of Botswana's Ministry of Health.

All patients hospitalized at Princess Marina Hospital between January 2000 and December 2007 and who had a blood culture that tested positive for *S. aureus* were eligible for inclusion; patients with MRSA were compared to those with methicillin-susceptible *S. aureus* (MSSA) bacteremia to identify risk factors for MRSA.

S. aureus bacteremia was defined as a blood culture yielding *S. aureus* as the sole pathogen. Polymicrobial blood cultures were not included. Multiple positive cultures performed on samples from the same patient within 7 days of the original culture were excluded. Hospital wards were categorized by the type of population treated in the ward.

Blood samples were processed using a Signal blood culture system (Oxoid). Isolation and identification of *S. aureus* were performed with Gram stain and coagulase test. Antimicrobial susceptibility patterns were determined with the disk diffusion method according to Clinical Laboratory Standards Institute guidelines. Methicillin or oxacillin susceptibility was determined after 24-hour incubation in Mueller-Hinton agar with 4% sodium chloride. To determine MRSA status, *S. aureus* was tested for susceptibility to methicillin from 2000 to 2005 and for susceptibility to oxacillin from 2006 to 2007. The D test for determining inducible resistance to clindamycin was not routinely performed.

Electronic and manual records of the Botswana National Health Laboratory were reviewed to identify bacteremic patients. Demographic data available included age, sex, and ward location at the time of sampling for blood culture. Patient HIV status and outcomes were not available. Because of personnel transitions and the shift from manual to electronic records, no laboratory records were available for December 2000 through May 2001 and March 2004 through October 2005. Because Princess Marina Hospital is a resource-constrained setting, blood culture bottles and antibiotics were periodically out of stock during the study period. The sporadic availability of blood culture bottles may have led to an underestimation of the burden of disease. Therefore, we report the proportion of patients with *S. aureus* bacteremia among all patients with bacteremia.

Continuous variables were described using mean, median, and range or interquartile range values and compared using the Wilcoxon rank sum test. Categorical variables were described using counts and percentages and compared using the Fisher exact test.

RESULTS

During the study period, 2,310 (29.7%) of 7,779 blood cultures tested positive for a single organism, with *S. aureus* being

TABLE. Demographic Characteristics of Patients with *Staphylococcus aureus* Bacteremia (n = 538)

Patient characteristic	No. (%) with MSSA	No. (%) with MRSA	Unadjusted odds ratio (95% CI)	P
Age group (n = 488) ^a				
<1 month	122 (44)	87 (41.2)	Reference	
1–11.9 months	41 (14.8)	34 (16.1)	1.2 (0.7–1.9)	.6
1 year–4.9 years	33 (11.9)	9 (4.3)	0.4 (0.2–0.8)	.02
5–14.9 years	25 (9)	8 (3.8)	0.4 (0.2–1)	.06
15–49 years	42 (15.1)	50 (23.7)	1.7 (1–2.7)	.04
≥50 years	14 (5)	23 (10.9)	2.3 (1.1–4.7)	.02
Sex (n = 455)				
Female	118 (45)	104 (53.9)	1.4 (1–2.1)	.01
Ward type (n = 517)				
Medical ward	123 (42.3)	92 (40.7)	Reference	
Surgical ward	27 (9.3)	17 (7.5)	1 (0.7–1.5)	.8
Neonatal intensive care unit	124 (42.6)	96 (42.8)	0.8 (0.4–1.6)	.6
Adult or pediatric intensive care unit	3 (1)	10 (4.4)	4.4 (1.2–16.6)	.03
Obstetrics and gynecology	4 (1.4)	7 (3.1)	2.3 (0.7–8.2)	.2
Oncology	3 (1)	1 (0.4)	0.4 (0.04–4.3)	.5
Accident and emergency	7 (2.4)	3 (1.3)	0.6 (0.1–2.3)	.4

NOTE. CI, confidence interval; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *S. aureus*.

^a Patient-specific information not available for all cases.

most commonly isolated. Antibiotic susceptibility results were available for 538 (92.4%) of 582 blood cultures in which *S. aureus* was the sole organism.

The Table displays the demographic characteristics of patients with *S. aureus* bacteremia and results of the univariate analysis. The cohort was 45% female, with a median age of 0.7 years (interquartile range, 0.02–23 years). Compared with

neonates, children aged 1–5 years had reduced odds of having MRSA, while adult subjects had increased odds of having MRSA, in both the 15–49 and the ≥50 years of age categories. Patients in the intensive care unit had increased odds of MRSA bacteremia compared with patients on the general adult medical wards. After adjusting for ward type, we found that the odds of MRSA bacteremia increased by 9% for each

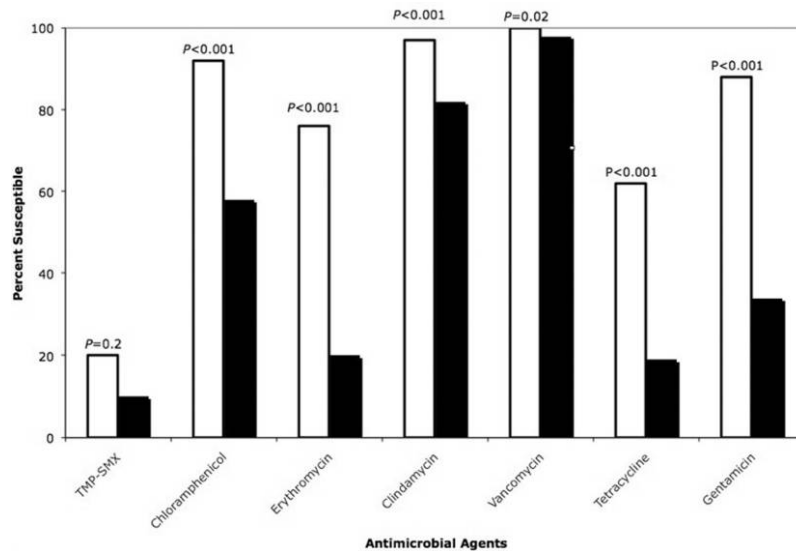


FIGURE. Antimicrobial susceptibilities of methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-susceptible *S. aureus* (MSSA) isolates. White bars represent percentage of MSSA isolates susceptible to each antimicrobial agent, while black bars represent percentage of MRSA isolates susceptible to that antimicrobial agent. Overall rates of susceptibility for specific antimicrobial agents were as follows: chloramphenicol, 77%; erythromycin, 51.3%; clindamycin, 90.8%; vancomycin, 99.2%; tetracycline, 43%; and gentamicin, 64.5%. For trimethoprim-sulfamethoxazole (TMP-SMX) sample size was insufficient to obtain a significant result.

5-year increase in age (adjusted odds ratio, 1.09; 95% confidence interval, 1.04–1.16; $P = .001$).

Of the 538 episodes of *S. aureus* bacteremia with known susceptibilities, 239 (44.4%) were caused by MRSA. The prevalence of *S. aureus* and MRSA bacteremia among all patients with confirmed bacteremia and known susceptibility results ($n = 2,129$) was 25.3% ($n = 538$) and 11.2% ($n = 239$), respectively. The median yearly proportion of MRSA among *S. aureus* isolates was 44.3% (range, 25.7%–58.3%), with the peak occurring in 2004.

S. aureus isolates were routinely tested for susceptibility to chloramphenicol, clindamycin, erythromycin, cephadrine, vancomycin, tetracycline, gentamicin, and methicillin (Figure). Susceptibility testing for trimethoprim-sulfamethoxazole was not routinely performed, and results were available for only 15 isolates. For trimethoprim-sulfamethoxazole susceptibilities, there was no significant difference between the MSSA and MRSA groups. MRSA isolates were significantly less susceptible to all other antimicrobial agents than were MSSA isolates. The large proportion of isolates resistant to erythromycin but susceptible to clindamycin suggests the possibility of inducible resistance to clindamycin.

DISCUSSION

Our study demonstrates several important findings about the epidemiologic characteristics of *S. aureus* bacteremia in Botswana. We found a high prevalence of bacteremia caused by *S. aureus*, and MRSA in particular, among patients at 1 hospital in an HIV-endemic region. We hope that these results will catalyze local changes in microbiologic and clinical practices to allow better surveillance and treatment of invasive *S. aureus* infections.

One of the most striking findings in this study is the overall high proportion of *S. aureus* bacteremia. In addition, almost half of the cases of *S. aureus* bacteremia were due to MRSA. We also identified several risk factors for MRSA among our cohort, including increased age and location in the intensive care unit. This finding is in keeping with previous reports, which described these risk factors.^{8,9}

Among MRSA isolates, we find high proportions of resistance to antimicrobials commonly used to treat *S. aureus* infections. Although more MRSA than MSSA isolates were resistant to clindamycin, the relatively high proportion of clindamycin susceptibility and erythromycin resistance among MRSA isolates raises the possibility of inducible clindamycin resistance. Although testing for trimethoprim-sulfamethoxazole was not common, high proportions of both MRSA and MSSA isolates that were tested were found to be resistant. Our results underscore the importance of introducing use of the D test for inducible resistance and of routine testing for resistance to trimethoprim-sulfamethoxazole in sub-Saharan Africa.

This study had several limitations. The prevalence of both

MRSA and MSSA bacteremia may have been underestimated due to the inconsistent availability of blood culture bottles. However, a lack of supplies is an unfortunate reality of medical care in the developing world. We were also unable to access patient-specific data other than age, sex, and ward. Therefore, we could not provide mortality data, differentiate between community-acquired and hospital-acquired infections, or group patients according to HIV status.

In summary, we report a high prevalence of both MRSA and MSSA bacteremia in Gaborone, Botswana. The high prevalence of MRSA and the increased proportions of resistance to commonly used antimicrobials among MRSA isolates call attention to the importance of revising antimicrobial susceptibility testing and empiric prescribing practices in Botswana.

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