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Major article

# Epidemiology of bloodstream infections caused by methicillin-resistant *Staphylococcus aureus* at a tertiary care hospital in New York

Mohamad Yasmin MD [a,*], Halim El Hage MD [a], Rita Obeid MA, MPhil [b], Hanine El Haddad MD [a], Mazen Zaarour MD [a], Ambreen Khalil MD [a]

[a] *Department of Internal Medicine, Staten Island University Hospital, Staten Island, NY*
[b] *The Graduate Center, City University of New York, New York, NY*

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***Background:*** In the United States, bloodstream infections (BSIs) are predominated by *Staphylococcus aureus*. The proportion of community-acquired methicillin-resistant *S aureus* (MRSA) BSI is on the rise. The goal of this study is to explore the epidemiology of BSI caused by *S aureus* within Staten Island, New York.

***Methods:*** This is a case-case-control study from April 2012-October 2014. Cases were comprised of patients with BSI secondary to MRSA and methicillin-sensitive *S aureus* (MSSA). The control group contained patients who were hospitalized during the same time period as cases but did not develop infections during their stay. Two multivariable models compared each group of cases with the uninfected controls.

***Results:*** A total of 354 patients were analyzed. Infections were community acquired in 76% of cases. The major source of BSI was skin-related infections (n = 76). The first multivariable model showed that recent central venous catheter placement was an independent infection risk factor (odds ratio [OR] = 80.7; 95% confidence interval [CI], 2.2-3,014.1). In the second model, prior hospital stay >3 days (OR = 4.1; 95% CI, 1.5-5.7) and chronic kidney disease (OR = 3.0; 95% CI, 1.01-9.2) were uniquely associated with MSSA. Persistent bacteremia, recurrence, and other hospital-acquired infections were more likely with MRSA BSI than MSSA BSI.

***Conclusion:*** Most infections were community acquired. The presence of a central venous catheter constituted a robust independent risk factor for MRSA BSI. Patients with MRSA BSI suffered worse outcomes than those with MSSA BSI.



Despite significant strides in antimicrobial therapy, *Staphylococcus aureus* continues to be implicated in a variety of infections ranging from superficial skin to deep-rooted life-threatening systemic infections.[1] In particular, morbidity and mortality rates remain elevated with *S aureus*—related bloodstream infections (BSIs) and infective endocarditis.[2-4] Methicillin-resistant *S aureus* (MRSA)—related bacteremia is associated with higher mortality, morbidity, and health care costs compared with that of methicillin-sensitive *S aureus* (MSSA).[5-7] Furthermore, the emergence of community-acquired MRSA in patients without the typically recognized risk factors has considerably altered therapeutic strategies and infection control practices in the hospital setting.[8,9] Although many infections secondary to *S aureus* have become manageable in recent times, the re-emergence of antibiotic resistance and community-acquired strains has maintained this pathogen's significance as a threat to public health.[10] This brings forth an array of obstacles that makes *S aureus* ever more difficult to treat. Some of these challenges include the decrease in glycopeptide susceptibility of MRSA and the looming threat of vancomycin-resistant *S aureus*.[8,10,11]

MRSA-related infections are considered to be a major public health concern around the world.[9] Based on data from the National Nosocomial Infections Surveillance System, the prevalence of invasive MRSA infections had all but doubled from 1996-2004.[12-16] In 2005, the Centers for Disease Control and Prevention (CDC)

* Address correspondence to Mohamad Yasmin, MD, 399 Naughton Ave, Staten Island, NY 10305.
*E-mail address:* myasmin@schoolph.umass.edu (M. Yasmin).
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underwent active monitoring of invasive MRSA infections through the Active Bacterial Core surveillance system within 9 U.S. cities.[17] During this 6-year surveillance, the CDC observed an increase in the overall proportion of invasive community-acquired and community-onset infections despite a decrease in the total number of invasive MRSA infections.[18] Multiple studies around the world have examined *S aureus* and MRSA bacteremia, albeit with significant variations in the reported incidence rates and described epidemiology. For instance, MRSA rates in Portugal and Italy had elevated to reach 54% and 58%, respectively.[19] In Japan around the same period in time, a staggering 70% of *S aureus* bloodstream cultures were resistant to methicillin in 2001.[20] In the United States, the incidence of *S aureus* bacteremia varies across ethnicities, age groups, and specific vulnerable populations. Some of these include hemodialysis patients, injection drug users, and individuals infected with HIV.[21]

The purpose of this study is to explore the epidemiology and complications of MRSA BSIs at Staten Island University Hospital (SIUH) in New York. Specifically, the study seeks to ascertain the unique risk factors that predispose to MRSA BSI and to determine whether those infections resulted in worse outcomes than MSSA.

## METHODS

### *Study location*

The study was conducted at SIUH, a specialized 714-bed tertiary care center located in New York City. It is a major referral center for the city of Staten Island serving a population of approximately 500,000 people with surgical, medical, pediatric, and obstetric care. SIUH contains specialized burn, cardiothoracic, and ventilator units along with 4 intensive care units (ICUs) and a dialysis center. The hospital serves a wide population of different socioeconomic classes from Brooklyn and Staten Island. According to published census results in 2010, the white population, including Italian ancestry, constitutes approximately 64% of Staten Island's inhabitants. The second largest group in Staten Island was of Hispanic origin, comprising 17% of the population as determined by the same census. Asian and black individuals formed the remaining major demographic breakdown in 7.4% and 9.5%, respectively.

### *Study design: cases and controls*

This is a case-case-control study designed to determine the risk factors and complications that are associated with MRSA BSI in patients admitted to SIUH from April 2012-October 2014. Patients included in the final analysis were distributed across 3 major groups. The first group of cases consisted of patients with MRSA BSI, whereas the second group were patients with MSSA BSI. The control group included patients hospitalized during the same time frame as cases but who did not contract infection during their hospital stay. A list of all positive blood cultures growing *S aureus* was provided by the microbiology laboratory. Adults >18 years of age who had a positive blood culture with *S aureus* on admission or during their hospitalization could be included in the final analysis. Patients with recurrent *S aureus* infections were encountered but could only be enrolled in the study once. The control group was made up entirely of uninfected patients who were also identified in a retrospective manner. Using a random integer generating software, controls were selected from a comprehensive list of patients provided by the medical records department. This group contained admitted patients who were hospitalized during the same time frame as cases but did not contract infection during their hospital stay. Two physicians reviewed the medical chart of each admission pertaining to a potential control to ensure eligibility into this category. Controls could therefore fall under any hospital service as long as it was determined that they remained free of infection during their stay.

### *Data collection*

Clinical data were collected from every patient's electronic medical chart using a comprehensive case report form. Laboratory and radiology software were also made available to ensure completion of data. The same case report form was used for patients with MRSA- and MSSA-related BSIs. The collected information consisted of basic demographics, comorbid medical conditions, treatment, and complications (including readmission and recurrence). Specifically, the data obtained included the following: age, sex, length of hospitalization, comorbid illnesses (malignancy, chronic obstructive pulmonary disease, chronic kidney disease [CKD], diabetes mellitus, etc), recent immune suppression, hemodialysis, HIV status, history of endocarditis, and intravenous drug abuse. Other potential risk factors pertaining to recent hospitalizations were also documented. These included central venous catheters (CVCs), urinary catheters, nasogastric tube insertion, mechanical ventilation, antibiotic use, surgery, prior hospitalization, and ICU stay. The Charlson Comorbidity Index was calculated for every patient to estimate illness severity and correlate with observed complications.

The study looked at complications that arose as a result of MRSA and MSSA BSIs. The following sequelae were analyzed for both case groups: sepsis, septic shock, acute kidney injury, cardiovascular event, cerebrovascular event, persistent bacteremia, prolonged hospital stay, ICU admission, other hospital-acquired infections, respiratory failure, and recurrent infection. These outcomes were considered present if they occurred after documentation of *S aureus* BSI and before discharge from the hospital. The assessment of recurrent MRSA or MSSA BSI was performed in the same manner consistent with the case-control study design. Patients' medical records and laboratory data were retrospectively inspected for *S aureus* BSI recurrence that occurred 6 months after their initial discharge date. All records of infection complications or recurrences were collected retrospectively, and patients were neither contacted by person nor phone for data collection beyond the study initiation date.

### *Definitions*

Variables were defined before the study was initiated. Bacteremia was considered hospital acquired when cultures were drawn >48 hours after admission.[22] In contrast, infection was designated as health care associated when it involved nursing home residents or patients receiving home or outpatient intravenous therapy, chemotherapy, wound care, or hemodialysis.[22] An absolute neutrophil count of <1,000 cells/mm$^3$ rendered patients as immune suppressed. Furthermore, an immune compromised state was also considered present if patients had received any immunesuppressive medication, radiation, or corticosteroids (analogous to 20 mg prednisone for at least 7 days) within 30 days of *S aureus* BSI. Patients were defined as having CKD if their glomerular filtration rate was <50 mL/min. Variables for infection acquisition, such as recent ICU stay, surgery, and prior hospital stay, were all considered to be risk factors within a time frame of 1 month from the occurrence of *S aureus* BSI. The placement of a nasogastric tube, urinary catheter, CVC, or mechanical ventilation was similarly documented when present within 1 month before infection. Information pertaining to antibiotic intake before a BSI caused by *S aureus* was collected in 2 separate variables. The first variable noted any exposure to antimicrobials for >48 hours within 30 days of infection while the second variable involved antibiotic use specifically