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Investigation of hospital-onset meticillin-resistant *Staphylococcus aureus* bloodstream infections at eight high-burden acute care facilities in the USA, 2016

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SUMMARY

Background: Despite large reductions from 2005 to 2012, hospital-onset meticillin-resistant *Staphylococcus aureus* bloodstream infections (HO MRSA BSIs) continue to be a major source of morbidity and mortality.

Aim: To describe risk factors for and underlying sources of HO MRSA BSIs.

Methods: This study investigated HO MRSA BSIs at eight high-burden short-stay acute care hospitals. A case was defined as first isolation of MRSA from a blood specimen collected in 2016 on or after hospital day 4 from a patient without an MRSA-positive blood culture in the preceding 2 weeks. Case demographics and risk factors were reviewed by medical record abstraction. The potential clinical source(s) of infection were determined by consensus by a clinician panel.

Findings: Of the 195 eligible cases, 186 were investigated. Cases were predominantly male (63%) and the median age was 57 years (range 0–92 years). In the 2 weeks preceding BSI, 88% of cases had indwelling devices, 31% underwent a surgical procedure and 18% underwent dialysis. The most common locations of attribution were intensive care units (ICUs) (46%) and step-down units (19%). The most commonly identified non-mutually exclusive clinical sources were central venous catheters (46%), non-surgical wounds (17%), surgical site infections (16%), non-ventilator healthcare-associated pneumonia (13%) and ventilator-associated pneumonia (11%).

Conclusions: Device- and procedure-related infections were common sources of HO MRSA BSIs. Prevention strategies focused on improving adherence to existing prevention bundles for device-and procedure-associated infections and on source control for ICU patients, patients with certain indwelling devices, and patients undergoing certain high-risk surgeries are being pursued to decrease the burden of HO MRSA BSIs at these facilities.

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Conflict of interest statement

None declared.

Keywords

Meticillin-resistant; *Staphylococcus aureus*; Bloodstream infection; Healthcare-associated; infections

Introduction

Meticillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infections (BSIs) are associated with high morbidity and mortality. In 2018, the most recent year for which data are available, there were 8222 hospital-onset (HO) MRSA BSIs reported to the National Healthcare Safety Network (NHSN) in the USA from inpatient units of acute care hospitals [1]. The national incidence of HO MRSA BSIs declined by 17% per year from 2005 to 2012 based on estimates from the US Centers for Disease Control and Prevention (CDC) Emerging Infections Program [2]. While it is difficult to attribute these declines to any single intervention or bundle of interventions, the data suggest that interventions to disrupt transmission of MRSA in acute care hospitals, as well as interventions to prevent central-line-associated bloodstream infections (CLABSIs), likely contributed [3–6]. Since 2013, there have not been significant changes in the incidence of HO MRSA BSIs [2].

Understanding the current epidemiology of HO MRSA BSIs has the potential to identify additional opportunities for further reductions, especially if the epidemiology of these infections has shifted as a result of prior prevention efforts. Interventions in high-burden short-stay acute care hospitals (SSACHs) have the potential to achieve the greatest absolute reduction in cases; therefore, this study reviewed cases of HO MRSA BSIs at eight high-burden SSACHs in two states in the USA to describe risk factors and determine the underlying sources of infection to inform targeted prevention strategies.

Methods

Facility selection

National surveillance for laboratory-identified healthcare-facility-onset MRSA bloodstream specimens in the USA is conducted through NHSN's Multidrug-Resistant Organism Module (protocol available at: https://www.cdc.gov/nhsn/PDFs/pscManual/12pscMDRO_CDADcurrent.pdf). Measures calculated for HO MRSA BSIs reported to NHSN include the standardized infection ratio (SIR) and the cumulative attributable difference (CAD). SIR is the ratio of the number of reported HAIs to the risk-adjusted number of predicted HAIs in a standard population, and CAD is the number of infections that must be prevented to reach an HAI reduction target. Statewide pooled CADs with a SIR goal of 0.5 were used to identify high-burden states; among these, both Kentucky and Tennessee had multiple high-burden facilities and state health departments with an interest in prioritizing MRSA HAI prevention activities. In total, five SSACHs from three healthcare systems in Kentucky and three SSACHs from three healthcare systems in Tennessee that had the highest MRSA CADs in their respective states in 2015 and continued to have high CADs in 2016 were included in the investigation.

Case identification

A case was defined as isolation of MRSA from a blood culture collected in 2016 on or after hospital day 4 from a patient without an MRSA-positive blood culture in the preceding 2 weeks. Cases were identified from clinical microbiology laboratory records; only medical records corresponding to a patient's index case, defined as the individual's first case in 2016, were reviewed. The hospitalization in which the index case was identified was designated as the index hospitalization.

Data collection

Medical records were abstracted by CDC and state Department of Health staff using a standardized form to collect patient demographics, social and past medical histories, microbiology results, presence of central venous catheters (CVCs) and other indwelling devices, receipt of dialysis, surgery and invasive procedures, wounds, and provider-determined sources (i.e. provider's impression of the underlying cause of MRSA BSI). Abstractors documented the presence of CVCs, arterial lines, midline catheters, endotracheal and nasotracheal tubes, surgical drains, tracheostomies and percutaneous feeding tubes, but not nasogastric or orogastric tubes or peripheral intravenous lines. Acute dialysis was defined as the receipt of dialysis in a patient without documentation of chronic outpatient dialysis at the time of admission. Surgery was defined as an incision made in the skin or mucous membrane performed in the operating room (OR); chest tube placements, tracheostomies and percutaneous endoscopic gastrostomy tube placements performed in an OR were included, and nevus removals and CVC placement were excluded. Wounds were defined as a break in the skin or mucous membrane caused by external damage or endogenous mechanisms that compromises the integrity of dermal or epidermal tissue. This included surgical wounds, blisters, bites, burns, cuts and abrasions, other traumatic wounds, pressure ulcers, diabetic ulcers, venous ulcers and arterial ulcers. Insertion sites for CVCs and other intravenous catheters were not considered wounds unless there was evidence of infection or malfunction at the insertion site. Surgical incisions from procedures such as tracheostomy placements, chest tube placements and surgical drains were classified as wounds. The unit of attribution for a BSI was defined as the unit or ward where the MRSA-positive blood culture was collected.

All abstraction forms were reviewed for accuracy, and missing or inconsistent data and any potential errors were resolved through re-review of medical records by each state's Department of Health.

Facility characteristics and general and MRSA-specific infection prevention practices were collected by telephone interview of key facility infection control staff using a standardized interview form.

MRSA infection source determination

The potential clinical source or sources for each BSI was determined through a consensus review process. Each case was reviewed by two CDC subject matter experts, and sources were categorized as single source identified, multiple sources identified or no source identified. Reviewers determined the source(s) (e.g. CVC) independently for each case. If

multiple potential sources were identified but one source was the most likely cause of infection, reviewers indicated this. Responses between the two reviewers were categorized as agreement when reviewers: (1) agreed on all sources selected; (2) agreed on the most likely source, when each reviewer chose multiple sources that were not identical; or (3) agreed on the most likely source, when one reviewer selected one source and the other reviewer selected this source as the most likely among multiple sources. In Scenario 2, all the selections that both reviewers had in common were reported as the source. In Scenario 3, only the source that both reviewers agreed was the most likely source was reported. Other responses were classified as disagreements. This included a subcategory of partial disagreement when reviewers agreed on at least one source but disagreed on the most likely source. All disagreements were adjudicated by a panel of five CDC subject matter experts.

For each potential infection source, the proportion of cases attributable to that source is expressed as a range. The numerator of the lower bound was limited to cases in which the infection source was the only source of infection identified; the numerator of the upper bound comprised all cases in which the source was identified, including cases for which multiple potential sources were identified.

This project was reviewed by the human subjects' advisors in the National Center for Emerging and Zoonotic Infectious Diseases at CDC, and was determined to constitute public health surveillance.

Data analysis

Data from abstraction forms were entered into a secure Access database (Microsoft Corp., Redmond, WA, USA), and data from the facility characteristics interview were entered into Excel (Microsoft Corp.). Descriptive analyses of facility-and patient-level data were conducted using SAS 9.4 (SAS Institute, Cary, NY, USA) and SPSS 21 (IBM Corp., Armonk, NY, USA).

Results

Facility characteristics

The eight participating SSACHs were teaching hospitals located in metropolitan areas. The median number of beds was 369 (range 292–1013), and the median number of adult intensive care unit (ICU) beds was 67.5 (range 34–185). Four facilities had a neonatal ICU (NICU), and the median number of NICU beds was 46.5 (range 10–70). Three facilities had a burns unit (median number of burns unit beds 9, range 5–14). Seven facilities reported having a policy to put known MRSA carriers in single rooms under contact precautions. Five facilities reported performing targeted MRSA admission screening: in NICUs (N=3); in adult ICUs (N=2); in newborn nurseries (N=1); for patients undergoing cardiac and joint replacement surgery (N=1); and for patients admitted from a long-term care facility (LTCF) (N=1).

Case characteristics

In total, 195 HO MRSA BSI cases were identified, of which 186 (95%; 98/98 from Kentucky and 88/97 from Tennessee) underwent chart review. The median age of cases at the time of index culture collection was 57 years (range 4 days–92 years), and 87 (47%) were aged between 45 and 64 years (Table I). Most cases were male (*N*=117, 63%) and non-Hispanic white (*N*=105, 57%). The median Charlson Comorbidity Index score was 2 (range 0–9); only one case without a documented underlying medical condition was identified. Overall, 35 (19%) patients had a documented history of MRSA infection or colonization in the year preceding positive blood culture.

Clinical course and outcomes of index hospitalization

The median duration of index hospitalization was 27 days (range 4–747 days) (Table I). The single patient with a 4-day hospitalization died on hospital day 4. The median time from admission to collection of the index culture was 11 days (range 4–392 days). Most cases (*N*=120, 65%) were admitted from a private residence; others were transferred directly from another SSACH (*N*=25, 13%), a LTCF (*N*=20, 11%), a long-term acute care hospital (LTACH) (*N*=6, 3%), jail (*N*=1, 1%), were homeless (*N*=1, 1%), or were admitted from other (*N*=7, 4%) or unknown (*N*=6, 3%) locations. CVCs were present on admission for 40 (22%) cases; of these, 20 (50%) were admitted from home, eight (20%) from a LTCF, seven (18%) from another SSACH, two (5%) from an LTACH, one (3%) from jail, and two (5%) from other locations.

In the 2 weeks preceding and up to the time of index culture collection (Table II), 164 (88%) patients had an indwelling device; CVCs were most common (*N*=134, 72%). One hundred and forty-four (77%) patients had a wound, 58 (31%) underwent surgery, and 34 (18%) underwent haemodialysis. Of the 144 cases with wounds, the most common wound types were surgical incisions (*N*=71, 49%), decubitus/pressure ulcers (*N*=32, 22%) and traumatic wounds (*N*=21, 15%). Among the 34 patients on haemodialysis, 29 (85%) received dialysis through a CVC and 19 (56%) received acute dialysis.

In the 2 weeks preceding the day before collection of the index culture, not including the day of BSI, 81 (44%) cases were admitted to an ICU. BSIs were most frequently attributed to ICUs (*N*=85, 46%) and step-down units (*N*=36, 19%). Overall, 51 (27%) cases died during hospitalization.

Clinical sources of HO MRSA BSIs

A single clinical source of infection was identified for 126 (68%) cases, 51 (27%) cases had multiple possible sources, and no source was identified for nine (5%) cases (Table III). The primary reviewers agreed on the clinical source(s) of infection in 152 (82%) of the 186 cases. Of the 34 remaining cases, 23 (68%) were classified as partial disagreement and 11 (32%) as complete disagreement. During adjudication of these 34 cases, 16 (47%) were determined to have multiple possible sources, 15 (44%) to have a single source, and three (9%) to have no identifiable source.

The most common sources of HO MRSA BSIs were CVCs (26–46% of cases), wounds excluding surgical site infections (SSIs) (10–17%), SSIs (8–16%), non-ventilator healthcare-associated pneumonia (5–13%) and ventilator-associated pneumonia (VAP) (1–11%) (Table III). Overall, 37–60% of cases had a device (CVC, indwelling urinary catheter or mechanical ventilator) or surgical procedure as the source.

Among 86 cases in which CVCs were identified as a possible source (single and multiple sources combined), 42 (49%) were from cultures collected in an ICU, 17 (20%) from cultures collected in a step-down unit, and 22 (26%) from patients who underwent dialysis in the preceding 2 weeks, of which 14 (64%) were inpatients who underwent acute dialysis. Among the 49 cases for which a CVC was the only identified source, 15 (31%) occurred within 7 days of catheter placement for all CVCs present, 27 (55%) occurred more than 7 days after catheter placement for all CVCs present, and seven (14%) occurred in patients who had more than one CVC present with at least one inserted more than 7 days and at least one inserted within 7 days preceding collection of the index culture. Among the 40 patients with CVCs present on admission, a CVC was the source of infection in 48–80% of cases.

Among the 32 patients with non-surgical wounds identified as a possible source, the most common types were burn wounds (*N*=13, 41%), chronic wounds (*N*=5, 16%) and traumatic wounds (*N*=5, 16%). These patients most commonly had their index culture collected in ICUs (*N*=17, 53%), followed by step-down units (*N*=5, 16%) and medical/surgical wards (*N*=3, 9%). Among the 30 patients with SSIs identified as a possible source, the most common types of surgery were gastrointestinal (*N*=11, 37%), amputation (*N*=5, 17%) and cardiothoracic (*N*=4, 13%). Half of these patients had their index culture collected in an ICU, and three (10%) had it collected on a surgical or medical/surgical ward.

Discussion

This review of 186 HO MRSA BSIs at eight high-burden SSACHs in two states found that cases tended to be older, male, have multiple co-morbidities and have long lengths of stay during hospitalizations where HO MRSA BSIs occurred. Collectively, BSIs were attributed to device- and procedure-related infections in 37–60% of cases. CVCs were most commonly identified as the source of infection, with up to 46% of all BSIs attributed to these devices. More than half of infections were attributed to non-ICU locations, most commonly step-down units. These results suggest that a substantial proportion of infections are related to medical devices and procedures for which evidence-based prevention bundles are available; augmenting these bundles with more novel strategies, such as source control during high-risk periods (e.g. while catheters are present), has the potential to drive further reductions.

The large reductions in HO MRSA BSIs observed from 2005 to 2012 represent a public health success story and were likely driven, in part, by expanded efforts to reduce CLABSIs and MRSA transmission in acute care settings [3–6]. Notably, the study data suggest that device- and procedure-related infections, including CLABSIs, remain a major cause of HO MRSA BSIs. This suggests that further implementation of, and adherence to, existing prevention bundles and evidence-based guidelines for device- and procedure-associated HAIs could result in further reductions in HO MRSA BSIs. Existing prevention resources

are available for intravascular catheter-related BSIs, VAP, catheter-associated urinary tract infections, haemodialysis-associated BSIs and SSIs.

Targeting interventions to inpatient unit types where cases commonly occur may also be a way to impact infection rates effectively. In this investigation, the two most common locations of attribution for cases were ICUs and step-down units. Patients in these units are often very ill, have multiple indwelling devices and wounds, and are at risk of severe complications from MRSA BSIs, making them high-priority locations for targeted interventions. However, infections also occurred on other unit types, including one-third of infections that were attributed to medical and surgical wards. This highlights the need to understand the local epidemiology when identifying unit types to target for intervention.

In addition to interventions focused on prevention of device- and procedure-associated infections, source control strategies, including use of topical and intranasal antiseptics/antibiotics, have shown promise in preventing MRSA BSIs. These interventions appear particularly beneficial for certain high-risk patients, including ICU patients, non-ICU patients with certain indwelling devices, and patients undergoing high-risk surgery. In the REDUCE MRSA trial, a universal source control strategy among ICU patients using topical chlorhexidine gluconate and intranasal mupirocin reduced MRSA clinical culture rates by 37% and all-cause BSIs by 44% [7]. The ABATE trial in a post-hoc analysis demonstrated that source control strategies resulted in a 30% reduction in MRSA infections among non-ICU patients with certain indwelling devices (CVCs, midline catheters and lumbar drains) [8]. Finally, pre-operative source control for surgical patients has been shown to be effective for SSI prevention for high-risk procedures such as orthopaedic, neurosurgical and cardiothoracic surgery [9–12]. Universal source control strategies for these three patient groups also have the potential to impact both MRSA and meticillin-susceptible *S. aureus* BSIs.

This investigation had several limitations. First, findings from these eight high-burden SSACHs in Tennessee and Kentucky are likely not completely generalizable to other facilities across the USA. In addition, results from the investigation are reported in aggregate and might not represent findings from an individual facility. Finally, although a standardized review process was developed to determine the clinical source objectively, including independent assessment by two expert reviewers and a consensus review process with five reviewers for instances of disagreement, the determination of clinical sources of BSIs was inherently subjective, particularly for infections such as pneumonia when supporting microbiologic evidence was not always available.

Despite large historical reductions in infection burden, HO MRSA BSIs continue to represent a significant cause of morbidity and mortality at hospitals across the USA. The epidemiology of infections at the eight hospitals in this evaluation suggests that prevention approaches that combine interventions to reduce MRSA transmission with interventions to reduce HAIs could result in further reductions, and these state health departments are working with the hospitals to ensure implementation of these interventions. CDC has published a list of evidence-based interventions that facilities can implement to prevent HO

MRSA BSIs (available at: https://www.cdc.gov/hai/prevent/staph-prevention-strategies.html) to assist healthcare facilities in reducing the incidence of these devastating infections.

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Table I

Demographics, clinical characteristics and hospitalization details of cases with hospital-onset meticillin-resistant *Staphylococcus aureus* bloodstream infections (HO MRSA BSIs)

Characteristic	*N* (%) unless otherwise specified
Total	186
Age (years)	
Mean	52.9
Median	57
Range	4 days-92 years
Sex	
Male	117 (62.9%)
Female	69 (37.1%)
Race/ethnicity	
Non-Hispanic white	105 (56.5%)
Non-Hispanic black	53 (28.5%)
Hispanic	6 (3.2%)
Non-Hispanic other	2 (1.1%)
Unknown	20 (10.8%)
Most frequent underlying medical conditions	
Diabetes mellitus	52 (28.0%)
Chronic pulmonary disease	43 (23.1%)
Chronic kidney disease	35 (18.8%)
Congestive heart failure	34 (18.3%)
CVA/stroke/TIA	30 (16.1%)
Duration of total hospitalization (days) (*N*=180)	
Mean	48.64
Median	27
Range	4–757
ICU stay in 2 weeks preceding BSI (not including day of BSI)	81 (43.6%)
Days from admission to HO	
MRSA BSI	

Characteristic	*N* (%) unless otherwise specified
Mean	20.4
Median	11
Range	4–392
≤1 week	56 (30.1%)
>1 week	130 (69.9%)
Unit of attribution	
ICU	85 (45.7%)
Neonatal ICU (*N*=85)	4 (4.7%)
Adult ICU (*N*=85)	81 (95.3%)
Step-down unit	36 (19.4%)
Medical ward	14 (7.5%)
Medical/surgical ward	14 (7.5%)
Other	14 (7.5%)
Oncology ward	12 (6.5%)
Surgical ward	5 (2.7%)
Unknown	6 (3.2%)
Hospitalization outcome	
Survived, discharged	134 (72.0%)
Died	51 (27.4%)
Unknown	1 (0.5%)

CVA, cerebrovascular accident; TIA, transient ischaemic attack; ICU, intensive care unit.

Denominators that are not 186 are indicated in first column as (*N*=).

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Table II

Healthcare exposures of patients in 2 weeks preceding hospital-onset meticillin-resistant *Staphylococcus aureus* bloodstream infections (MRSA BSIs)

Characteristic	*N* (%), *N*=186[a]
CVC or other indwelling device[b] present in 2 weeks preceding MRSA BSI	164 (88.2%)
CVC present in 2 weeks preceding MRSA BSI (*N*=164)	134 (81.7%)
Midline catheter or arterial line present in 2 weeks preceding MRSA BSI (*N*=164)	56 (34.2%)
Received invasive mechanical ventilation in 2 weeks preceding first MRSA BSI	81 (43.5%)
Underwent surgical procedure in 2 weeks preceding MRSA BSI	58 (31.2%)
Underwent dialysis in 2 weeks preceding MRSA BSI (*N*=185)	34 (18.4%)
Dialysis type (*N*=34)	
Haemodialysis	34 (100%)
Dialysis access (*N*=34)	
CVC	29 (85.3%)
Arteriovenous fistula	5 (14.7%)
Wound present in 2 weeks preceding MRSA BSI	144 (77.4%)

CVC, central venous catheter.

[a]Denominators that are not 186 are indicated in first column as (*N*=).

[b]Indwelling devices included CVCs, arterial lines, midline catheters, endotracheal and nasotracheal tubes, surgical drains, tracheostomies and percutaneous feeding tubes, but not nasogastric/orogastric tubes or peripheral intravenous lines.

Table III

Clinical sources of 186 hospital-onset meticillin-resistant *Staphylococcus aureus* bloodstream infections

Characteristic	Single source or no identifiable source (lower bound) *N* (%)	Single and multiple combined source or no identifiable source (upper bound) *N* (%)
Total	135 (72.6%)	186 (100%)
No identifiable source	9 (4.8%)	9 (4.8%)
CVC	49 (26.3%)	86 (46.2%)
Wounds (not including surgical incisions)	19 (10.2%)	32 (17.2%)
SSI and surgical wounds	15 (8.1%)	30 (16.4%)
Pneumonia (non-VAP)	9 (4.8%)	24 (12.9%)
Pneumonia (VAP)	2 (1.1%)	21 (11.3%)
Recurrence of prior infection	8 (4.3%)	10 (5.4%)
Peripheral intravenous line	7 (3.8%)	8 (4.3%)
Abscess	2 (1.1%)	6 (3.2%)
Other[a]	2 (1.1%)	2 (1.1%)
Gastrointestinal tract[b]	3 (1.6%)	5 (2.7%)
Indwelling urinary catheter	2 (1.1%)	3 (1.6%)
Other indwelling device[c]	5 (2.7%)	7 (3.8%)
Injection drug use	2 (1.1%)	3 (1.6%)
Arteriovenous fistula/graft	1 (0.5%)	2 (1.1%)
Other[a]	2 (1.1%)	2 (1.1%)
No identifiable source	9 (4.8%)	9 (4.8%)

CVC, central venous catheter; VAP, ventilator-associated pneumonia.

[a]Other sources included cellulitis with gangrene (*N*=1) and septic arthritis/bursitis (*N*=1).

[b]Gastrointestinal sources included necrotizing enterocolitis (*N*=1), peritonitis following a gastrointestinal bleed (*N*=1), translocation related to Crohn's disease (*N*=1), translocation related to pancreatitis and a duodenal ulcer (*N*=1), and perforated sigmoid diverticulitis (*N*=1).

[c]Other indwelling devices included chest tube (*N*=3), midline catheter (*N*=2), external jugular catheter (*N*=1), and arterial line or intraosseous line (*N*=1).