HHS Public Access

Author manuscript

J Am Geriatr Soc. Author manuscript; available in PMC 2024 April 12.

Published in final edited form as:

J Am Geriatr Soc. 2018 August ; 66(8): 1581–1586. doi:10.1111/jgs.15451.

Burden of Invasive Methicillin-Resistant *Staphylococcus aureus* Infections in Nursing Home Residents

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Abstract

OBJECTIVES: To describe the epidemiology and incidence of invasive methicillin-resistant *Staphylococcus aureus* (MRSA) infections in nursing home (NH) residents, which has previously not been well characterized.

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Author Contributions: All authors made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data, drafting the article or revising it critically for important intellectual content, and final approval of the version to be published. Conception and drafting: Cheri Grigg, Nimalie Stone, Isaac See, Data Acquisition: Cheri Grigg, Danielle Palms, Nicole Gualandi, Wendy Bamberg, Ghinwa Dumyati, Lee H. Harrison, Ruth Lynfield, Joelle Nadle, Susan Petit, Susan Ray, William Schaffner, John Townes, Isaac See, Analysis: Cheri Grigg, Danielle Palms, Interpretation & revising: All authors.

Conflict of Interest: No relevant conflicts of interest.

DESIGN: Retrospective analysis of public health surveillance data.

SETTING: Healthcare facilities in 33 U.S. counties.

PARTICIPANTS: Residents of the surveillance area.

MEASUREMENTS: Counts of NH-onset and hospital-onset (HO) invasive MRSA infections (cultured from sterile body sites) identified from the Centers for Disease Control and Prevention Emerging Infections Program (EIP) population-based surveillance from 2009 to 2013 were compared. Demographic characteristics and risk factors of NH-onset cases were analyzed. Using NH resident-day denominators from the Centers for Medicare and Medicaid Services Skilled Nursing Facility Cost Reports, incidence of NH-onset invasive MRSA infections from facilities in the EIP area was determined.

RESULTS: A total of 4,607 NH-onset and 4,344 HO invasive MRSA cases were reported. Of NH-onset cases, median age was 74, most infections were bloodstream infections, and known risk factors for infection were common: 1,455 (32%) had previous MRSA infection or colonization, 1,014 (22%) had decubitus ulcers, 1,098 (24%) had recent central venous catheters, and 1,103 (24%) were undergoing chronic dialysis; 2,499 (54%) had been discharged from a hospital in the previous 100 days. The in-hospital case-fatality rate was 19%. The 2013 pooled mean incidence of NH-onset invasive MRSA infections in the surveillance area was 2.4 per 100,000 patient-days.

CONCLUSION: More NH-onset than HO cases occurred, primarily in individuals with known MRSA risk factors. These data reinforce the importance of infection prevention practices during wound and device care in NH residents, especially those with a history of MRSA infection or colonization.

Keywords

methicillin-resistant *Staphylococcus aureus*; nursing home; invasive infections; epidemiology

Methicillin-resistant *Staphylococcus aureus* (MRSA) causes an estimated 80,461 invasive infections and 11,285 deaths per year in the United States and is a leading cause of healthcare-associated infections.[1] The U.S. Department of Health and Human Services identified reduction of healthcare-associated invasive MRSA infections as a national priority in the National Action Plan to Prevent Healthcare Associated Infections.[2] Most MRSA prevention strategies have been implemented in acute care hospitals, with substantial success in preventing MRSA infections in U.S. hospitals over the past decade,[3] but 80% of invasive MRSA infections occur outside hospitals, with more than 60% of cases occurring within 12 weeks after hospital discharge.[3] A recent study examining risk factors for invasive MRSA found that admission to a nursing home (NH) was an independent risk factor for invasive MRSA infection after discharge from an acute care hospital, even when controlling for the presence of more typical risk factors for MRSA infection.[4]

Approximately 4 million individuals receive care in 15,600 NHs each year in the United States.[5] The NH population is changing as more post-acute care residents are admitted for short-term rehabilitation and skilled care. For example, from 2000 to 2010, the number of short-stay NH residents in New York State increased by more than 75%.[6] Many of these residents enter the NH with indwelling medical devices, wounds, a history of

systemic antimicrobial administration, or MRSA colonization, each of which are risk factors associated with invasive MRSA infection.[4,7–13] Therefore, individuals receiving short-stay, post-acute care in NHs may be a large population at risk of serious infection. Previous studies examining MRSA in NH residents have focused on prevalence of and risk factors for colonization[7,14–16] and have reported high rates of MRSA colonization, but the incidence of invasive MRSA infections in NH residents has not been reported. We describe the burden of NH-onset invasive MRSA infections in a diverse geographic area within the United States and demographic, clinical, and healthcare exposure characteristics of affected residents.

Human Subjects Considerations

The MRSA surveillance protocol underwent human subjects review at the Centers for Disease Control and Prevention (CDC) and was determined to be a nonresearch activity. Participating sites obtained human subjects and ethics approvals from academic partners and state health department review boards as applicable. This data analysis was also considered to be a nonresearch activity after review by the human subjects liaison at the National Center for Emerging and Zoonotic Infectious Disease, CDC.

METHODS

Surveillance System

We analyzed data reported to the CDC Emerging Infections Program (EIP) surveillance system for invasive MRSA infections from January 1, 2009, to December 31, 2013. This is an active population- and laboratory-based surveillance system that has been previously described.[17] The analysis includes data only up to 2013 because, at the time the analysis was conducted, 2013 denominator data used to calculate NH incidence (described in more detail below) were the most recent available. From 2009 to 2013, the system covered a population of 19 million persons from 33 counties in 9 states (California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New York, Oregon, Tennessee). Trained surveillance personnel at each participating site investigated all laboratory reports of MRSA isolated from normally sterile body sites of residents in their catchment area. Demographic and clinical data were obtained from medical record review, and a standard case report form was completed.

Case Definitions

EIP defines a case as MRSA isolated from a normally sterile body site (e.g., blood, cerebrospinal fluid, internal body fluid) in a surveillance area resident. Persons receiving care in NHs are considered to be residents of the area where the facility is located. Data reported were used to determine whether cases could be epidemiologically classified as NH-onset or hospital onset (HO). NH-onset cases were defined as cases for which the individual had resided in a freestanding inpatient rehabilitation facility, skilled nursing facility, NH, or inpatient hospice 4 calendar days before the MRSA culture collection date. HO cases were those in which the culture was obtained more than 3 calendar days after hospital admission. An individual could represent more than 1 case if he or she had 2 or more positive cultures more than 30 days apart.

Descriptive Epidemiology of Invasive MRSA Infections

Case counts and clinical characteristics of NH-onset and HO cases from EIP surveillance data were compared. Demographic and clinical data were analyzed, including age, sex, underlying medical conditions, previous healthcare exposures, and clinical syndromes associated with culture. The Charlson Comorbidity Index was calculated in two different ways: one incorporating age as a prognostic indicator, and the other excluding age as a prognostic indicator, as described in previous publications.[18,19] Data on NH length of stay for cases was not available. For NH-onset cases with prior hospitalization in the year before culture, the distribution of time from hospital discharge to positive culture was described. Because Medicare provides short-stay coverage for NH residents for up to 100 days, the percentage of NH-onset cases occurring within 100 days of hospital discharge was calculated as a proxy for the proportion of cases occurring in short-stay residents.

Statistical Methods

Characteristics of NH-onset and HO cases were compared using the chi-square test for dichotomous measures (alpha=.05). Age and Charlson Comorbidity Index scores of NH-onset and HO cases were compared using the Wilcoxon-Mann-Whitney test (alpha=.05).

A pooled mean incidence of NH-onset invasive MRSA infections for NHs in the EIP catchment area was calculated for each of the 9 EIP sites for 2013. The numerator was the number of NH-onset cases reported to EIP in 2013. The denominator was the total number of NH resident-days in all NHs located in each catchment area summed to create a single denominator value for each EIP site. A complete list of NHs within the EIP MRSA catchment area was obtained from the Centers for Medicare and Medicaid Services (CMS) Provider of Services files.[20] Information on NH resident-days was obtained from CMS Skilled Nursing Facility Cost Reports,[21] which all NHs with licensed skilled nursing beds participating in the Medicare program submit annually, and from CMS Hospital Cost Report inpatient data for NHs with cost reports filed under affiliated hospitals. Inpatient day data was imputed using the SAS Proc MI procedure based on bed count and EIP site for NHs with missing inpatient data (8% of included NHs) (SAS Institute, Inc., Cary, NC). For NHs reporting patient-days for less than the length of time they were in operation during a fiscal year (4% of included NHs), resident-days counts for the entire operational period were extrapolated based on reported use. The pooled mean incidence of NH-onset MRSA bloodstream infections (BSIs) was calculated from EIP data by limiting the numerator to cases in which MRSA was isolated from a blood culture and using a NH resident-day denominator as described above.

Data analysis was performed using SAS version 9.3.

RESULTS

Demographic and Clinical Characteristics

From 2009 to 2013, there were 4,607 NH-onset invasive MRSA cases and 4,344 HO cases in catchment-area residents. Fifty-six percent of the NH-onset cases were male, 59% were white, and 31% were younger than 65 (Table 1). The most common underlying medical

comorbidities in NH-onset cases were diabetes mellitus (51%) and renal insufficiency (43%). Dementia was reported in 29% of NH-onset cases and decubitus ulcers in 22%.

The predominant infection type was BSI (91% of cases), of which 41% were BSI without other infection types reported. Ninety-two percent of NH-onset cases were hospitalized, 13% had septic shock recorded in their medical record, and 19% died during hospitalization. Demographic and clinical characteristics of NH-onset and HO invasive MRSA cases are shown in Table 1. In general, NH-onset cases were older, and more likely to have underlying medical conditions, including septic shock (13%, 592 cases).

Healthcare risk factors

Hospitalization in the prior year was the most common healthcare exposure for NH-onset cases, occurring in 73% of cases (n=3,356). Of those cases, 79% (n=2,499) developed an invasive MRSA infection within the first 100 days after hospital discharge (Figure 1).

Eighty percent of NH-onset cases had prior hospitalization or atleast1 of the following healthcare exposures: previous MRSA colonization or infection (32%), surgery within 1 year of culture (29%), chronic dialysis (24%), and central venous catheter within 2 days of positive culture (24%).

Incidence of NH-Onset Invasive MRSA Infections

The EIP MRSA catchment area included 777 NHs. The median number of NH beds per facility was 108 (range 5–769); 213 NHs (27%) had fewer than 75 beds. The median number of NH resident-days in 2013 was 34,111 (range 3,088–277,442). The number of NHs per EIP site ranged from 22 to 231 (Table 2).

In 2013, the incidence of NH-onset invasive MRSA infections per EIP site ranged from 1.4 to 5.6 cases per 100,000 resident-days (Table 2). The pooled mean incidence of NH-onset invasive MRSA from all sites was 2.8 cases per 100,000 resident-days, with a pooled mean of 1.2 cases per NH annually. The pooled mean incidence of NH-onset MRSA BSI was 2.4 per 100,000 NH resident-days.

DISCUSSION

Although other studies have described prevalence of and risk factors for MRSA colonization in NHs, this is the first large-scale description of invasive MRSA infections occurring in NH residents. More NH-onset than HO cases were reported in the EIP catchment area. As what might be typically expected for HO cases, NH-onset invasive MRSA infections were severe, with high frequency of hospitalization, development of septic shock, and death.

NH residents developing invasive MRSA infections were younger than the national NH population (<65: 31% vs 15%) and more likely to be male (56% vs 33%).[23] This is consistent with other literature describing male sex as a risk factor for MRSA colonization and BSI.[24] The proportion of NH-onset cases with dementia (29%) contrasts with the prevalence of dementia in NH residents nationally (50%).[25] In addition, 24% of the NH-

onset cases had a central venous catheter in place, although only 2% of NH residents nationally receive intravenous medications.[26]

The younger age of MRSA cases and high prevalence of intensive healthcare exposures suggests that these cases are not primarily occurring in the traditional long-term residential population but instead may be occurring in the growing population of NH residents admitted for short-stay, post-acute care. The timing of onset of these infections supports this; of residents with hospital discharge in the past year, 79% of infections occurred within the first 100 days of admission to the NH, and 30% occurred within the first 30 days.

In addition to describing the epidemiology of invasive MRSA infections, this the first study to report the incidence of NH-onset invasive MRSA infections. Although the epidemiology suggests that post-acute care residents may have a different level of risk of invasive infection, a single incidence rate was calculated for the entire NH population. The EIP MRSA surveillance system does not currently collect data on NH length of stay for case-patients, but in the United States, the short-stay population is much smaller than the long-stay NH population,[5] and most of our cases were discharged from acute care hospital stays within 100 days. Therefore, the actual incidence of invasive MRSA in short-stay NH residents may be substantially greater than the incidence we calculated for all NH residents.

The pooled mean incidence of 2.8 invasive MRSA cases per 100,000 resident-days would translate to approximately 0.82 cases per year in a NH with 100 beds and 80% occupancy, although this calculation would correctly predict MRSA burden only if one assumed the incidence of MRSA in NH residents was the same in NHs with different characteristics and in different regions. In contrast, we noted substantial variation in NH-onset invasive MRSA infection incidence according to EIP site. Investigating reasons for the differences in incidence according to facility-level characteristics (e.g., proportion of long-stay and short-stay residents) or according to site (e.g., acuity of NH care in different sites, variation in MRSA prevalence in hospitals discharging individuals to NHs) might uncover additional opportunities for prevention. Although the mean number of cases per NH is small, there may be individual NHs in which invasive MRSA infections are more common and in which efforts to prevent MRSA should be prioritized. Therefore, determining the variation in NH-onset invasive MRSA incidence within an EIP site might also be important for targeted prevention work.

As our results suggest, improving infection prevention practices during care of residents with risk factors such as indwelling medical devices and recent invasive procedures might reduce the burden of invasive MRSA in NHs. The CDC supports efforts of health departments and partners to implement activities shown to prevent MRSA infections and transmission between NH residents, such as strengthening infection prevention practices for residents with central venous catheters through staff education, monitoring adherence to hand hygiene and gown and glove use, and conducting surveillance for infections and multidrug-resistant organisms.[27,28] Given that the onset of many invasive MRSA infections is within the first 100 days after hospital discharge, efforts to communicate presence of MRSA risk factors during transitions from hospitals to NHs may also improve care and reduce the occurrence of invasive MRSA infections in NH residents.

Our analysis has several limitations. First, the incidence of NH-onset invasive MRSA from the EIP catchment area may not reflect the incidence elsewhere in the United States. Second, because these data were analyzed in aggregate without being linked to specific NHs, we were unable to assess infection rates at the facility level, nor could we capture data on facility infection prevention programs or staffing. Additionally, a small proportion of our NH-onset cases may be from other long-term care facility types. Third, NH length-of-stay data are not collected as part of the EIP MRSA surveillance system, so we did not have denominator data stratified according to long- versus short-stay residents. We are unable to precisely define incidence according to short and long stay. Notable strengths of this project include coverage of different geographic regions and inclusion of data that represent many (>700) NHs.

CONCLUSION

Current professional society guidelines for preventing MRSA transmission and infection focus on the hospital setting,[11] and HO invasive MRSA has declined substantially over the past decade.[3,29] We found that, in residents of geographically diverse regions, the number of cases of NH-onset invasive MRSA exceeded that of HO invasive MRSA. These data support the need for greater attention to prevention of NH-onset invasive MRSA infections and coincide with identification of long-term care facilities as a priority setting for strengthening infection prevention and antibiotic stewardship efforts as part of the national plan to combat antibiotic-resistant bacteria.[30,31] In addition, if the growth of post-acute care in NHs in recent years continues, the burden of invasive MRSA infections in this setting may continue to grow.

The CDC, building on efforts to strengthen infection prevention programs in NHs, is expanding strategies to improve practices during care of residents with wounds, devices, or a history of MRSA who may be at greater risk of invasive infection. Calculating NH-onset invasive MRSA incidence is an important step for monitoring prevention efforts in this setting. Future efforts for the EIP include determining regional and facility-specific factors that could account for variation in NH-onset invasive MRSA infection rates and targeting regional prevention measures through identification of facilities that may have higher rates of infections.

ACKNOWLEDGMENTS

The authors would like to thank CDC staff members James Baggs and Yi Mu for analysis and database assistance; Anthony Fiore and Shelley Magill for critical feedback and discussion of results; the CDC EIP office for administrative support; and the following EIP site staff for data collection and project oversight at sites: Lauren Pasutti, Brittany Martin, Cindy Amezcua, Gretchen Rothrock, Arthur Reingold, Elizabeth Partridge, Maria Rosales (California EIP); Deborah Aragon, Claire Reisenauer, and Kenneth Gershman (Colorado EIP); Carmen Marquez, Michelle Wilson, and Heather Altier (Connecticut EIP); Randy Van Dolson, Sasha Harb, Stepy Thomas, Monica M. Farley, Wendy Baughman, Amy Tunali, Janine Ladson, Jessica Reno, Betsy Stein, and Lewis Perry (Georgia EIP); Terresa Carter, Rosemary Hollick, Kathleen Shutt, Joanne Benton, Kim Holmes, Janice Langford, and Lindsay Bonner (Maryland EIP); Kathryn Como-Sabetti, Mackenzie Koeck, and Jessica Nerby (Minnesota EIP); Anita Gellert, Christina Felsen (New York EIP); Heather Jamieson, Tasha Poissant, Mark Schmidt, and Jamie Thompson (Oregon EIP); and Gail Hughett, Terri McMinn, Brenda Barnes, Karen Leib, and Katie Dyer (Tennessee EIP).

Financial Disclosure:

This work was supported by a cooperative agreement through the CDC EIP (Grants U50CK000201 [California], U50CK000194 [Colorado], U50CK000195 [Connecticut], U50CK000196 [Georgia], U50CK000203 [Maryland], U50CK000204 [Minnesota], U50CK000199 [New York], U50CK000197 [Oregon], U50CK000198 [Tennessee]).

The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of the CDC.

Sponsor's Role:

The CDC oversaw all aspects of the study other than subject recruitment and directly determined the design, methods, analysis, and preparation.

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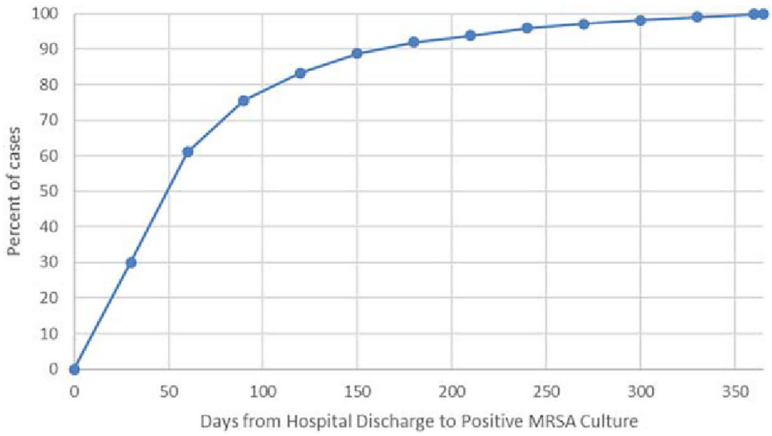

Figure 1.

Days from hospital discharge to onset of illness (positive MRSA culture) among persons with nursing home-onset invasive methicillin-resistant Staphylococcus aureus (MRSA) infection within one year following hospital discharge 2009–2013 (n=3,181).[a]

[a]Data unavailable for 275 cases.

Table 1.

Demographic and Clinical Characteristics of Nursing Home (NH)-Onset and Hospital-Onset (HO) Invasive Methicillin-Resistant *Staphylococcus aureus* (MRSA) Cases: 2009–2013

Characteristic	NH-Onset, n = 4,607	HO, n = 4,344
Age, median (range)	74 (20–103)	61 (18–98)
Aged <65, n (%)	1,405 (30.5)	2,480 (57.1)
Male, n (%)	2,575 (55.9)	2,593 (59.7)
Race, n (%)[1]		
White	2,701 (58.6)	2,429 (55.9)
Black	1,407 (30.5)	1,398 (32.2)
Other	147 (3.2)	119 (2.8)
Underlying medical conditions, n (%)[2]		
Diabetes mellitus	2,325 (50.5)	1,749 (40.3)
Renal Insufficiency	1,986 (43.1)	1,252 (28.8)
Dementia	1,336 (29.0)	348 (8.0)
Stroke	1,064 (23.1)	506 (11.7)
Decubitus ulcer	1,014 (22.0)	499 (11.5)
Peripheral vascular disease	760 (16.5)	505 (11.6)
Cancer	634 (13.8)	790 (18.2)
Obesity	552 (12.0)	625 (14.4)
Charlson Comorbidity Index, mean ± SD	3.0 ± 2.1	2.4 ± 2.1
Charlson Comorbidity Index, incluing age, mean ± SD	5.8 ± 2.4	4.2 ± 2.8
Type of infection associated with culture, n (%)[2]		
Bloodstream	4,194 (91.0)	3,121 (71.9)
Bloodstream alone	1,723 (41.0)	1,649 (52.4)
Pneumonia	875 (20.9)	622 (19.9)
Urinary tract	396 (9.4)	152 (4.9)
Bone or joint	350 (8.4)	151 (4.8)
Pressure ulcer or chronic wound	310 (6.7)	217 (5.0)
Catheter site	285 (6.2)	149 (3.4)
Cellulitis	278 (6.0)	332 (7.6)
Incision or surgical site	244 (5.3)	211 (4.9)
Abscess (not skin)	157 (3.4)	269 (6.2)
Healthcare exposure, n (%)	3,770 (80.2)	3,263 (75.1)
Hospitalization ≤ 1 year before culture	3,356 (72.8)	2,538 (58.4)
Previous MRSA infection or colonization	1,455 (31.6)	1,160 (26.7)
Surgery ≤ 1 year before culture	1,356 (29.4)	1,658 (38.2)
Chronic dialysis	1,103 (23.9)	507 (11.7)
Central venous catheter ≤ 2 days before culture	1,098 (23.8)	1,517 (34.9)
Outcome, n (%)		
Hospitalization	4,230 (91.8)	

Characteristic	NH-Onset, n = 4,607	HO, n = 4,344
Septic shock	592 (12.9)	342 (7.9)
Death	860 (18.9)	890 (20.5)

All comparisons of demographic and clinical characteristics between NH-onset and HO cases were statistically significant (alpha = .05) except pneumonia, surgical site or incision infection, and death.

[1] Race unknown for 352 NH-onset cases (7.6%) and 398 HO cases (9.2%).

[2] Infection types and underlying conditions were not mutually exclusive

Table 2.

Number of Nursing Homes (NHs), NH Resident-Days, and NH-Onset Invasive Methicillin-Resistant *Staphylococcus Aureus* Incidence Per Emerging Infections Program (EIP) Site: 2013

EIP Site	Nursing Homes, n	NH Resident-Days	Cases, n	NH-Onset Incidence Per 100,000 Resident-Days
California	121	3,891,807	105	2.70
Colorado	89	2,838,676	47	1.66
Connecticut	231	9,292,293	210	2.26
Georgia	68	3,205,792	136	4.24
Maryland	72	3,114,799	171	5.49
Minnesota	84	3,193,840	45	1.41
New York	33	1,568,674	38	2.42
Oregon	57	1,371,760	20	1.46
Tennessee	22	804,786	34	4.22
Total	777	29,282,427	806	2.75