Major Article

Prevalence of and outcomes from *Staphylococcus aureus* pneumonia among hospitalized patients in the United States, 2009-2012

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Background: The burden of *Staphylococcus aureus* pneumonia is unknown despite being a major cause of mortality. We investigated national estimates of methicillin-resistant *S aureus* (MRSA) and methicillin-susceptible *S aureus* (MSSA) pneumonias and predictors of in-hospital mortality and hospital length of stay (LOS).

Methods: This was a retrospective analysis of the National Inpatient Sample from 2009-2012. Adult patients with an ICD-9-CM primary diagnosis code for MRSA or MSSA pneumonia were included. Data weights were used to derive national estimates. Prevalence rates were reported per 100,000 hospital discharges, with trends presented descriptively.

Results: There were 104,562 patients who had a primary diagnosis of *S aureus* pneumonia, with 81,275 from MRSA. MRSA pneumonia prevalence decreased steadily from 2009 (75.6 cases per 100,000 discharges) to 2012 (56.6 cases per 100,000 discharges), with MSSA pneumonia experiencing a slight decrease. Mortality rates decreased between 2009 and 2012 for MRSA pneumonia (7.9% to 6.4%) and MSSA pneumonia (6.9% to 4.7%; $P = .008$). LOS was higher for MRSA (6.9-7.8 days) compared with MSSA (6.1-6.4 days).

Conclusions: The prevalence of MRSA pneumonia has decreased among hospitalized adults in the United States in recent years accompanied by improvements in mortality and LOS. Although the prevalence of MRSA pneumonia is declining, national vigilance is still warranted.

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Lower respiratory tract infections in general and pneumonias in particular are major causes of mortality in the United States. According to the Centers for Disease Control and Prevention, there were 53,282 deaths attributable to pneumonia across all ages in 2013, making it the leading cause of infection-related death.[1] *Staphylococcus aureus* pneumonia presents as community, hospital-acquired, and health care–associated,[2-4] and 20%-40% of all hospital-acquired and ventilator-associated pneumonias can be attributed to methicillin-resistant *S aureus* (MRSA).[4] Although relatively uncommon causes of community-acquired pneumonia, methicillin-sensitive *S aureus* (MSSA) and MRSA are important emerging respiratory pathogens in the community, with MRSA pneumonia associated with severe necrotizing infection, especially after influenza.[5,6] Regardless of the setting, the epidemiology and national estimates of *S aureus*, MSSA, and MRSA pneumonias are unknown.

Identifying risk factors for infection with *S aureus* is important because delaying treatment with the most appropriate antibiotics may increase mortality. Conversely, overuse of antibiotics can lead to antibiotic-related complications, including the emergence of multidrug-resistant organisms.[7-9] Specific known risk factors for MSSA and MRSA pneumonias include recent hospitalization, recent intravenous antibiotic administration, tobacco use, and chronic obstructive pulmonary disease.[10-12] The identification of other patient-related or hospital-level factors contributing to such infections and patient outcomes would be useful to inform prevention policies in healthcare settings and to develop an evidence base on how to allocate resources and adjust health care policies to address this issue.

National estimates and infection trends are useful statistics to improve the assessment of invasive MRSA pneumonia infection in the United States and provide evidence on the magnitude of the problem. Therefore, the primary objectives of this study were to estimate the prevalence of and describe outcomes from *S aureus*, MRSA, and MSSA pneumonias in the United States using the Nationwide Inpatient Sample (NIS). Our secondary objectives were to identify predictors of in-hospital length of stay (LOS) and mortality within this population. We hypothesized that MRSA pneumonia is associated with more adverse outcomes.

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Conflicts of interest: None to report.

METHODS

Data source

The NIS contains data on discharges and is annually developed by the Agency for Healthcare Research and Quality for the Healthcare Cost and Utilization Project.[13] It is the largest publicly available all-payer hospital discharge database in the United States, containing data on approximately 8 million hospital stays and formed from a 20% stratified random sample of all acute care hospitals in the United States. Up to 2011, the sampling design included community hospitals as the primary sampling units and all discharges from those hospitals. In 2012, the NIS was redesigned as a sample of discharges from all participating hospitals. Because of the inclusion of stratification and weighting variables, users can apply data weights to derive national estimates and trends.

In 2012, the sample included 1,050 hospitals in 44 states providing data on a multitude of patient- and hospital-level characteristics. The variables include the following: demographics (age, race, and sex), insurance status (Medicare, Medicaid, private insurance plans, uninsured, and other insurance plans), and primary diagnosis codes (identified from ICD-9-CM diagnosis codes). Primary diagnosis codes were used here to reduce misclassification because pneumonia is a difficult diagnosis and MRSA is a common sputum colonizer.[14] Prior to 2009, 15 diagnosis codes were available for each patient, thereafter extended to 25 diagnosis fields. The first-listed diagnosis was regarded as the condition chiefly responsible for the patient's admission to hospital for care. Additional variables included geographic region of the hospital as defined by the U.S. Census Bureau (Northeast, South, Midwest, or West), indicators for 29 different comorbid conditions, median household income, and hospital size (small, medium, or large).

Study design

This was a retrospective analysis of adult patients discharged from U.S. hospitals within the NIS database from 2009-2012. Patients were included if they were aged ≥18 years and had a primary diagnosis code for MSSA (482.41) or MRSA pneumonia (482.42). ICD-9-CM codes were updated in October 2008 to include both MSSA and MRSA pneumonias. To minimize misclassification because of under- or overutilization of a new code, we included only the years 2009-2012 in our analysis.

Data and statistical analysis

Descriptive statistics were used to define patient and hospital characteristics. The main outcome variables included the prevalence rates for *S aureus* pneumonia (overall *S aureus* pneumonia [a composite value of MRSA and MSSA pneumonia diagnoses] and stratified by diagnosis of MRSA or MSSA pneumonia), in-hospital mortality (IHM), and hospital LOS. The annual prevalence rates for *S aureus* pneumonia were determined using *S aureus* pneumonia discharges as the numerator and total discharge estimates from the Agency for Healthcare Research and Quality estimates of hospital use as the denominator. Data weights were applied to derive national estimates, and prevalence rates are presented as hospitalizations per 100,000 total adult discharges. IHM was identified by the discharge status item of the NIS, which represents all-cause IHM. Hospital LOS was extracted from the LOS item of the NIS and was presented as a median (interquartile range) given the positive data skew.

Multivariate logistic regression was used to examine the association between patient- and hospital-level characteristics and IHM. MRSA was used as a primary independent variable of interest. Odds ratios and 95% confidence intervals (CIs) were computed for each independent variable. To examine the association between potential patient- and hospital-level factors and LOS, a multivariate linear regression model was constructed in which the occurrence of MRSA was one of the primary independent variables. Because of the positive skew of LOS, data were log-transformed including the LOS estimate. A positive regression estimate represents an increased LOS, and a negative estimate represents a decreased LOS. In both models examining the association between multiple independent variables and outcomes, hospitalizations with missing information were excluded. Furthermore, within the linear regression model, patients that died within their hospital stay were also excluded to minimize bias in LOS outcome. Simple linear regression was applied to assess prevalence and outcome trends during the study period. All model characteristics were assessed for multicollinearity using variance inflation factors (VIFs); 2 variables were considered highly correlated if they had a VIF >10. Statistical significance was assessed at an a priori α level of 0.05. All analyses were 2-sided and conducted using SAS Version 9.4 (SAS Institute, Cary, NC).

RESULTS

A total of 9,656,915 hospitalizations involved pneumonia during the study period: 104,562 had a primary diagnosis code of *S aureus* pneumonia, of which 77.7% were MRSA. The characteristics of patients with *S aureus* pneumonia are summarized in Table 1. Most

Table 1
Baseline characteristics of adults with *Staphylococcus aureus* pneumonia in the United States, 2009-2012

Characteristic	Total pneumonia (N = 9,656,915)	*S aureus* pneumonia (n = 104,562)
Infection		
MRSA	0.84	77.7
Age, y		
18-39	7.2	7.6
40-65	30.6	28.4
>65	62.2	64.0
Sex		
Female	51.4	50
Male	48.6	50
Ethnicity		
White	66.7	72.1
Black	11.6	7.7
Hispanic	6.9	5.3
Asian or Pacific Islander	1.8	1.7
Native American	0.6	0.7
Other	2.3	1.7
Median household income		
$1-$38,999	31.4	33.1
$39,000-$47,999	25.8	26.9
$48,000-$62,999	22.4	21.5
$63,000	17.9	16.2
Primary payer		
Medicare	66.1	70.9
Medicaid	9.9	10.3
Private, including HMO	17.2	13.4
Self-pay	3.9	2.8
No charge	0.4	0.4
Other	2.2	2.0
Hospital size		
Small	15.2	16
Medium	25.3	24.4
Large	58.6	58.7
Hospital region		
Northeast	18.1	14.4
Midwest	23.8	22.8
South	40.2	44.5
West	17.8	18.4

NOTE. All data are presented as proportion of patients (%).
HMO, Health Maintenance Organization; *MRSA*, methicillin-resistant *S aureus*.