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Risk Factors for Community-Onset
Methicillin-Resistant *Staphylococcus aureus* Bacteremia

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Risk Factors for Community-Onset Methicillin-Resistant *Staphylococcus aureus* Bacteremia

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An abstract of
A thesis submitted to the Faculty of the
James T. Laney School of Graduate Studies of Emory University
in partial fulfillment of the requirements for the degree of
Master of Science
in Clinical Research
2011

ABSTRACT

Risk Factors for Community-Onset
Methicillin-Resistant *Staphylococcus aureus* Bacteremia
By Jesse T. Jacob

The characteristics and risk factors for bacteremia with methicillin-resistant *Staphylococcus aureus* (MRSA) at the time of admission to an acute care hospital have not been well characterized after the recent changes in MRSA epidemiology. All charts for adults with *S. aureus* in blood cultures obtained within 48 hours of admission (community-onset, CO) were reviewed over a five year period, with only the first episode of *S. aureus* bacteremia per patient included in the analysis. Patients with MRSA bacteremia were classified as cases, and those with methicillin-sensitive *S. aureus* (MSSA) were used as the comparison group. Patients with CO MRSA bacteremia had a median age of 59.4 (range: 37.1-87.2) and were 94.8% male and 48.8% black. The most common co-morbidity was diabetes mellitus (54.4%). Patients with CO MSSA bacteremia had similar demographic and clinical characteristics. Among the 84 cases and 58 comparators, there were similar rates for prior culture positivity with MSSA (6.0% vs. 5.2%), but only cases had prior positive culture with MRSA (14.3% vs. 0%, $p<0.01$). Frequency of hospitalization was higher among cases (53.6% vs. 31.0%, $p=0.01$). In univariate analysis, the major definable predictors of CO MRSA bacteremia were receipt of oral (OR 3.19, $p<0.01$) and intravenous (OR 2.78, $p<0.01$) antibiotics as well as prior hospitalization (OR 3.19, $p<0.01$). For patients who were previously hospitalized, the OR for was 7.42 if they had received IV antibiotics, compared to 0.85 if they had not received IV antibiotics ($p=0.01$). In multivariate analysis, the single greatest predictor of CO MRSA bacteremia was hospitalization in the last 90 days among patients receiving antibiotics (OR 6.12, $p=0.01$). Among those who did not receive antibiotics, no single variable predicted outcome. Post-hospitalization surveillance interventions may be important considerations in developing prevention strategies. Antimicrobial stewardship may also pray a crucial role in decreasing the burden of MRSA bacteremia on the healthcare system.

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ACKNOWLEDGEMENTS

I am indebted to the many individuals who directly or indirectly helped to bring this to fruition, especially those in the MSCR program, Emory University's Division of Infectious Diseases, the Centers of Disease Control and Prevention's Division of Healthcare Quality Promotion and the Pittsburgh Regional Health Initiative. Special thanks to Jenny Luke for chart abstraction with meticulous attention to detail and insightful comments, David Rimland for obtaining the line listing, and John Jernigan for mentoring me through this process. Finally and most importantly, I wish to thank my wife Natasha for her patience and support.

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INTRODUCTION

Bacteremia with methicillin resistant S. aureus (MRSA) is associated greater lengths of hospital stay, higher mortality [1] and increased costs [2] even when compared with methicillin sensitive S. aureus (MSSA) and certainly more than with patients without such infections. These infections have frequently been associated with healthcare delivery and are usually considered exclusive to the healthcare setting. Current hospital-based infection surveillance systems usually attribute infections incubating at the time of admission (considered community-onset) as being acquired from outside the hospital. Given the frequency with which patients interact with the healthcare system, including hospitals, long-term care facilities, nursing homes and other settings, these definitions probably underestimate the true incidence of infection associated with healthcare. The epidemiology of bacteremia with MRSA at the time of admission needs to be further characterized to determine the relative importance of prior healthcare exposure and other risk factors.

This study examines the epidemiology of community-onset *S. aureus* bacteremia in a single acute care hospital over a five year period to quantify the characteristics of patients with MRSA bacteremia and identify risk factors, particularly those associated with healthcare, for MRSA when compared to MSSA.

BACKGROUND

Staphylococcus aureus, a virulent pathogen implicated in a broad spectrum of human disease ranging from mild skin and soft tissue infections to life-threatening bloodstream infections, continues to pose a significant public health problem in the US. The burden of invasive MRSA infections remains significant; the Centers for Disease Control and Prevention's (CDC) Active Bacterial Core surveillance (ABCs) system estimated in 2005 there were 94,360 cases of invasive MRSA infections contributing to 18,650 deaths in the US.[3]

For the last ten years, the epidemiology of MRSA has been rapidly changing. Until the last decade, MRSA was considered a hospital-acquired pathogen causing severe invasive disease, most commonly from bacteremia. In 2003, MRSA first appeared in the community causing outbreaks of skin and soft-tissue infections in previously healthy individuals with little or no exposure to the hospital [4]. These infections had distinct genotypic and phenotypic characteristics, possessing a staphylococcal cassette chromosome (SCC) mec type IV or V, the Panton-Valentine leukocidin and the USA300 pulsotype, in contrast to the classic hospital-acquired strains of MRSA which were typically mec type II, USA100 or USA200 pulsotypes, and lack the Panton-Valentine leukocidin [5].

Recently the distinction between community-acquired and hospital-acquired infections has been blurred, and USA300 MRSA strains have been found to be associated with healthcare-acquired infections. As part of assessment of MRSA's burden in the US, the nearly 9,000 invasive MRSA infections in ABCs from 2005 were classified as healthcare associated or community associated [3]. Healthcare-associated infections were

defined as cases with an invasive device at the time of admission, history of MRSA infection or colonization, or history of surgery, dialysis or residence in a long-term care facility in the prior year, or a culture positive after 48 hours after admission to the hospital. Community-associated infections had none of those risk factors. Healthcare-associated infections were also stratified by time of onset. Positive cultures obtained within 48 hours of hospital admission were classified as community-onset (CO) healthcare-associated infections; positive cultures drawn more than 48 hours of hospitalization were considered hospital-onset healthcare-associated infections. Unsurprisingly, most (85%) cases of invasive MRSA infections were healthcare-associated, but a majority of all infections (58%) were CO, suggesting that they were associated with the delivery of healthcare but had their onset outside of the acute hospital stay. Interestingly CO healthcare-associated infections outnumbered both community-associated or hospital-onset healthcare-associated cases. This raises the hypothesis that CO invasive MRSA infections are related to events occurring during prior encounters with healthcare.

Molecular typing among patients bacteremic on admission has shown that genotypic strains were those typically associated with healthcare. Further evidence of the association of prior healthcare exposure in CO MRSA bloodstream infections can be found in the MRSA Prevention Initiative Pilot Study, which used data from a multi-center regional healthcare improvement initiative based in Pittsburgh to determine the frequency of prior hospitalizations in patients with CO MRSA bacteremia from December 1998 to October 2007 at 10 VA centers. In 1,808 cases, 226 (24.7%) cases had inpatient stays within four weeks, 883 (48.89%) had inpatient stays within 16 weeks

and two-thirds had inpatient stays within one year. The study showed an stepwise association between recent hospital discharge and CO MRSA bacteremia, lending further support to the idea that CO bacteremia was likely healthcare-associated[6].

This study seeks to describe the epidemiology of patients admitted with CO MRSA bacteremia admitted to a single VA center to ascertain the risk factors for MRSA bacteremia, hypothesizing that more recent and more acute healthcare exposure is associated with an increased risk for CO MRSA bacteremia compared to CO MSSA bacteremia.

METHODS

This study was designed to test the null hypothesis that among patients admitted to an acute care VA medical center with CO *S. aureus* bacteremia, patients with MRSA bacteremia have statistically equal frequency of more recent hospitalization within 1 year compared patients bacteremic with MSSA. Additionally, the study sought to describe the epidemiologic characteristics of patients with CO MRSA bacteremia, particularly in their exposures to healthcare within the hospital and outside the hospital.

Setting

The Atlanta VA Medical Center (VAMC) is a 142 bed hospital in Decatur, Georgia and is the only inpatient VA facility in the metropolitan Atlanta area. It serves as a referral center for the network of VA clinics and houses several medical and surgical subspecialty clinics as well as primary care. The Emory University Institutional Review Board and the VAMC Research and Development Committee approved this study. Two pre-existing VAMC databases were used to generate a list of eligible patients. The infectious diseases database was used to identify all patients with *S. aureus* bacteremia. This line list was cross-referenced with the admissions/discharge/transfer database identify patients with CO *S. aureus* bacteremia.

Case and Comparisons Selection

All adults (> 18 years of age) admitted to the VAMC between January 1, 2005 and November 1, 2008 with CO bacteremia with *S. aureus* were included. CO bacteremia was defined as *S. aureus* isolated from blood cultures obtained within 48 hours before or after admission. Patients with MRSA on the initial admission blood culture were considered cases; those with MSSA were used as comparators. Only the

first episode of CO *S. aureus* bacteremia was included for analysis. Patients whose index admission was the entry into the VAMC were excluded since this limited the timeframe of medical records available for review.

Chart Review

A structured questionnaire was completed for each patient, and data were extracted from the VAMC's electronic medical records, including all clinical notes and laboratory sections up to one year prior to the index admission. In addition to demographics, clinical information on the current bacteremic episode included methicillin susceptibility and recent healthcare exposures. Dates of recent visits to outpatient clinics, emergency rooms, surgical procedures and non-surgical invasive procedures were recorded. Time from event (i.e. for hospitalization or surgery) was calculated by subtracting the index event date from the last event date; for example the time from last hospitalization was obtained by subtracting the index discharge date from the second readmission date. Time from event variables were stratifying by intervals; for example the primary predictor variable of hospitalization in last 90 days was given a value of 1 if a patient had a time from last hospitalization between 0 and 90, and a value of 0 if the time from last hospitalization was greater than 90 or not previously hospitalized. Other potential healthcare exposures including intravenous (IV) and oral (PO) antibiotic use, hemodialysis, presence of central venous catheter (CVC) at time of admission or within last year were also noted. Co-morbidities required to calculate the modified Charlson score were identified by reviewing all admission and discharge summaries for 1 year prior to admission bacteremia; the standard methodology for Charlson scoring was modified by considering all liver disease in the mild to moderate

category and assuming that all diabetes did not have complications, giving a maximum possible modified Charlson score of 20 instead of the maximum unmodified Charlson score of 22.

Statistical Analysis

Continuous variables were assessed using measures of center and spread (mean, standard deviation, median and range). Ordinal variables were assessed using frequencies. Identification of risk factors for methicillin resistance in CO *S. aureus* was initially assessed by univariate analysis using the Chi-square test or Fisher's exact test. A p value of less than 0.05 was considered significant, and all p values less than 0.10 were reported. Interaction was assessed using the Breslow-Day test, and collinearity using the Collins Macro. Variables associated with methicillin resistance in the univariate analysis and selected pre-determined variables were included in multivariate logistic regression analysis. Several models were examined including a full model with all variables and a model reduced to variables found significant by univariate examination. Two different sets of post-hoc sensitivity analyses were done: one excluding all patients with prior clinical MRSA cultures and the other excluding all patients with bacteremia in 2008. All statistical analyses were carried out using SAS version 9.2 (Cary, NC)

RESULTS

Of the 169 episodes of CO *S. aureus* bacteremia identified during the study period, 104 (61.5%) were methicillin-resistant and 65 (38.5%) were methicillin-sensitive. Four episodes (2 MRSA, 2 MSSA) were excluded because insufficient medical records were available, and 23 episodes were excluded because they represented second (21) or third (2) episodes, leaving 84 cases and 58 comparisons for analysis.

Description of Cases

Patients with CO MRSA bacteremia had a median age of 59.4 (range: 37.1-87.2) and were 94.8% male and 48.8% black (Table 1). The most common co-morbidity was diabetes mellitus (54.4%); the presence of liver disease (20.4%), chronic kidney disease requiring hemodialysis (15.5%) and HIV (9.5%) in this population was notable. The median modified Charlson score was 3 (range: 0-10).

Most patients had accessed healthcare frequently in the form of hospitalization (72.6%), clinic visits (96.4%) or ER visits (81.9%). Among previously hospitalized patients (n=62), the median number of hospitalizations was 2 (range: 1-10) and total length of stay during all hospitalization was 11 (range: 1-162), while the median number of days since last hospitalization was 41 (range: 2-350). For visiting an outpatient clinic, the median number of visits of 12.5 (range: 1-58). The majority of these visits were to medical or medical subspecialty clinics compared to surgical, rehabilitation or other clinic settings. Stay in a long-term care facility was infrequent (15.5%).

Many had undergone invasive procedure (81.0%) or surgeries (46.3%). Most surgeries were orthopedic (33.3%), vascular (28.2%), or abdominal (25.6%), where as most procedures involved placing central access (44.1%) or for cardiovascular

diagnostics or therapeutics (19.1%). More than a third of patients had a CVC placed in the last year, 26.2% had a CVC present on their index admission. The majority (84.5%) of cases had IV or PO antibiotics in year prior to the index admission.

MRSA had previously been isolated from 26.2% of cases. The clinical team attributed the site of CO bacteremia to wounds or skin (31.0%) or unknown/unclear sites (28.6%) for most cases (Table 2). CVC was the third most common site (22.6%), though split nearly in half by hemodialysis and non-hemodialysis line-types. Fewer CO MRSA bacteremias appear to occur in 2008 compared to the other years ($p<0.01$, figure 2). Many veterans (26/84 or 31.0%) had undergone a prior hospitalization, surgery or invasive procedure outside of the VA system within a year of their index admission.

Cases and Comparators

Cases and comparators shared similar demographics and co-morbidities (Table 2). Approximately half the patients in both groups had diabetes and a modified Charlson score >2. HIV was more common in the MRSA group than comparators (9.5% vs. 1.7%, $p=0.08$). Antibiotic exposure was more common 90 days prior to admission among the cases, whether through the intravenous (53.6% vs. 29.3%, $p<0.01$) or oral (78.6% vs. 53.4%), $p<0.01$) route. While there were similar rates for prior culture positivity with MSSA (6.0% vs. 5.2%), only cases had prior positive culture with MRSA (14.3% vs. 0%, $p<0.01$). Among the other healthcare exposures, only hospitalization (53.6% vs. 31.0%, $p=0.01$) was statistically different, though the rates for stay in a long-term facility (15.5% vs. 8.6%, p=NS) and surgery (28.6% vs.15.5%, $p=0.07$) were nearly double for cases. CO MRSA bacteremia occurred with more frequency after a recent hospitalization, with more than half of all cases hospitalized in the past 3 months. By comparison, half of all

patients with CO MSSA bacteremia had been hospitalized in the last 7 months (Figure 3). Fewer cases of MRSA occurred in 2008 compared to prior years compared to MSSA.

Univariate and Multivariate Analysis

In univariate analysis (Table 3), the major definable predictors of CO MRSA bacteremia were oral (OR 3.19, 95% CI: 1.53-6.65, p<0.01) and IV (OR 2.78, 95% CI: 1.37-5.68, p<0.01) antibiotics as well as prior hospitalization (OR 3.19, 95% CI: 1.53-6.65, p<0.01). The OR for prior MSRA culture positivity was undefined since no patients in the comparison group had prior MRSA. Among the other predictors, recent surgery (OR 2.18, 95% CI: 0.93-5.11, NS), stay in a long term care facility (OR 1.94., 95% CI: 0.65-5.75, NS), and HIV (OR 6.00, 95% CI: 0.73-49.34, NS) were more common with CO MRSA BSI though the association was not statistically significant.

Interaction between hospitalization and IV antibiotics was detected. For patients who were hospitalized, the OR for was 7.42 if they had received IV antibiotics, compared to 0.85 if they had not received IV antibiotics (p=0.01). There was no evidence of interaction with any of the other predictors (Table 4). By visual inspection, no collinearity was detected among all of the variables in the univariate analysis.

Several different multivariate models were constructed. In the simplest model (Table 5) the 3 significant predictors from univariate analysis were entered, with the exception of IV antibiotics. Oral antibiotics (OR 3.82, 95% CI: 1.39-10.52, p<0.01) and hospitalization (OR 2.80, 95% CI: 1.09-7.17, p=0.03 both predicted outcome. In the next model (Tables 6A and 6B), the outcome was stratified by IV antibiotics to account for interaction. Among patients receiving IV antibiotics, while oral antibiotics no longer predicted outcome (OR 1.24, 95% CI: 0.21-7.26, p=NS), hospitalization emerged as a

potent predictor (OR 5.77, 95% CI: 1.44-23.44, p=0.01). There were no significant predictors of outcome in patients who had not received IV antibiotics. A more complex model (Tables 7A and 7B) incorporating the other healthcare associated risk factors (CVC on admission, long term care stay, ER visit, surgery and invasive procedure) showed that hospitalization remained the strongest predictor of CO MRSA bacteremia among patients who had received IV antibiotics (OR 7.67, 95% CI 1.20-49.14, p=0.03). Several parameters such as CVC on admission, surgery, and invasive procedures in the IV antibiotic strata, had OR less than 1 in this model, compared to OR greater than 1 in univariate analysis.

In the third model (Tables 8A and 8B), only 4 terms were entered into the model, stratified by IV antibiotics: oral antibiotics, hospitalization, and long term care stay. In this model, the single greatest predictor of CO MRSA bacteremia was hospitalization in the last 90 days among patients those receiving antibiotics (OR 6.12, 95% CI: 1.50-25.00, p=0.01). Among those who did not receive antibiotics, no single variable predicted outcome. Sensitivity analysis of this model removing all patients with prior MRSA did not change the model significantly (Tables 9A and 9B). An additional sensitivity analysis excluding all episodes of bacteremia in 2008 yelled similar results (Tables 10A and 10B).

DISCUSSION

For over 50 years, MRSA has been an important pathogen confined to the healthcare setting. Our data show MRSA bacteremia occurring early in the hospitalization and traditionally attributed to the community is associated with prior healthcare exposure, specifically associated with previous hospitalization within 3 months and previous receipt of IV antibiotics, compared to patients with MSSA bacteremia.

Well-described risk factors for MRSA bacteremia include prolonged hospitalization, treatment in the intensive care unit, antibiotic exposure, surgery, and prior cultures with MRSA, all exposures directly related to healthcare [7]. In this study, many of these risk factors were associated with the outcome of methicillin resistance in univariate analysis. Controlling for other variables in multivariate analysis, two prominent risk factors emerged: hospitalization and exposure to IV antibiotics. The combination of these two risk factors was a potent predictor of methicillin resistance (OR 6.12). Without exposure to IV antibiotics, recent hospitalization was not associated with outcome.

Other studies have sound a strong association with antibiotic use and methicillin resistant *S. aureus* infections [8-10]. Although IV antibiotics may be initiated in the outpatient setting, IV antibiotics are often started in the hospital for suspected infection and typically include a fluoroquinolone or a β-lactam, inducing selection pressure for methicillin resistance among *S. aureus* [11]. Use of these agents may be associated with increased rates of invasive MRSA [12]. A computer-generated intervention to decrease fluoroquinolone use in a VA hospital was associated with decreased MRSA rates,

suggesting that this and other approaches to antibiotic stewardship may be effective in combating MRSA [13]. In a single center, quasi-experimental study, modification in prescribing of third-generation cephalosporins and ciprofloxacin decreased consumption and lowered MRSA bacteremia rates while MSSA bacteremia rates remained stable [14]. Another opportunity for antibiotic stewardship is de-escalation, since antibiotic use is frequently empiric but prolonged despite accumulating clinical data against the role of infection. Antibiotic stewardship, usually in concert with infection control practices, may be leveraged to reduce MRSA bacteremia in the hospital setting; these practices likely need to be extended through the spectrum of healthcare, from clinic to the acute care hospital to long term care facilities.

Hospitalization is a recognized risk factor the acquisition of MRSA. Transmission of healthcare associated pathogens such as MRSA frequently occurs in the hospital, but can occur in the clinic, emergency room, and other facilities such as long term acute care facilities or skilled nursing facilities acting as a social network. Several recent studies have assessed the role of transmission of pathogens through networks of healthcare. Though frequently assumed to be closed system, in this population, nearly a third (31.0%) of patients with CO MRSA bacteremia had a recent hospitalization, surgery or invasive procedure outside the VA system documented in clinical notes. This may under represent the true incidence of important healthcare exposure outside the VA system. Patients can stay in nursing homes, skilled nursing facilities, acute long term acute care facilities and short-term acute care hospitals during a relatively short period of time and these transfer can affect transmission of MRSA [15].

Hospitalization can be a risk factor for MRSA since healthcare serves as a reservoir. MSSA is more common in the general population (28.4%) compared to MRSA (1.5%); while invasive rates of MRSA are decreasing, healthcare associated bacteremias decreased at a lower rate and remain more common than hospital-onset bacteremias [16, 17]. Not surprisingly, the combination of antibiotic pressure in a setting with increased prevalence is the major risk factor for MRSA bacteremia. These results are consistent with the reported literature. Prior hospitalization has also been found to be significant risk factor [3, 6, 10, 18]. As many as 70% of patients admitted with CO hospital-acquired MRSA bacteremia had been hospitalized at least once in the preceding year [9].

Notable in this study was the lack of association with some of the risk factors described in the literature, such as admission to a long-term care facility, high Charlson co-morbidity scores, diabetes mellitus, renal insufficiency, malignancy, and the presence of indwelling CVC on admission [9, 19, 20]. Differences in these risk factors may be explained by the use of MSSA bacteremia as the comparison groups, whereas many studies use enteric pathogens which have different pathophysiology compared to *S. aureus*. The balanced distribution of demographics and co-morbidities suggests that the selection of MSSA as a comparison group is appropriate.

One potentially important risk factor, prior clinical cultures with MRSA, could not be included in the model since it was present only in patients with CO MRSA bacteremia but not in patients with CO MSSA bacteremia. This coupled with the observation that both groups had the same rates of prior clinical cultures with MSSA suggests that previous MRSA clinical cultures are a major risk factor for MRSA

bacteremia, consistent with several prior studies in patients with healthcare-associated infections [21-23]. This study excluded surveillance cultures for MRSA. In the VAMC, active surveillance for MRSA began in October 2008 as part of a national directive.

Though the number of CO MSSA bacteremia remained stable, the number of CO MRSA bacteremia in 2008 declined compared to earlier years. Data from 2009 and early 2010 suggest that the number of CO MRSA bacteremia episodes rose again in 2009 and 2010 to levels similar to those seen between 2005 and 2007, suggesting that the observed decrease in 2008 was annual variation (D. Rimland, personal communication). To make the model more generalizable, year was not included in logistic regression, and sensitivity analysis excluding episodes in 2008 revealed no differences.

There are some limitations to this study. Data was obtained from a chart review in patients admitted to a single VA institution over a five year period. Although many of the findings are consistent with previous reports, the data may not be representative of all populations. Despite a 5 year time frame, the number of episodes of *S. aureus* is modest; this may led to lower power in detecting differences between the groups. This may in part account for some lack of association of the outcome with some risk factors frequently cited in the literature and have resulted in overfitting of the second model. Because no patients with MSSA bacteremia had previous cultures positive for MRSA, this potentially important risk factor could not be included in the multivariate model. Finally, information in the medical record may not have been complete, especially with healthcare exposure outside the VA system. Many patients had undergone surgeries, invasive procedures or hospitalization in non-VA healthcare facilities and more may have

occurred that would not have been captured unless documented in the VA medical records.

Despite these limitations, these data contribute to the emerging evidence that MRSA is associated with healthcare delivery. Recent hospitalization and IV antibiotic use in combination were strong predictors of MRSA. Most healthcare-associated infection surveillance systems currently used by hospitals measure only those infections having their onset during the hospital stay, therefore bloodstream infections that have their onset post-discharge are less likely to be captured. Our data suggest that post-hospitalization surveillance interventions may be important considerations in developing prevention strategies. Rational use of antibiotics, guided by the principles of antimicrobial stewardship, may also pray a crucial role in decreasing the burden of MRSA bacteremia on the healthcare system.

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TABLES and FIGURES

Table 1: Selected Characteristics of Patients with Community-Onset Methicillin-resistant *S. aureus* (MRSA) Bacteremia

Characteristic	MRSA (n=84)	
	n	%
Age in years, median (range)	59.4 (37.1-87.2)	
Male	81	94.8
Black race	41	48.8
Charlson score, median (range)	3 (0-10)	
Diabetes mellitus	44	52.4
Hemodialysis	13	15.5
HIV	8	9.5
Liver Disease	17	20.4
Antibiotics	71	84.5
Prior MRSA	22	26.2
Hospitalization	61	72.6
Median (range)	1 (0-10)	
Days since last discharge	29 (2-284)	
Prior total length of stay	15 (1-162)	
Long term care facility	13	15.5
CVC (admission)	22	26.2
ER visits	68	81.9
Median (range)	1 (0-21)	
Clinic visits	81	96.4
Median (range)	13 (0-58)	
Invasive Procedures	68	81
CVC	30	35.7
Cardiac	13	15.5
Biopsy	10	11.9
Incision and drainage	10	11.9
Endoscopy	9	10.7
Other	9	10.7
Surgery	39	46.3
Orthopedic	13	15.5
Vascular	11	13.1
General	10	11.9
Urology	6	7.1
Cardiac	3	3.6
Other	3	3.6

CVC: central venous catheter
ER: emergency room
HIV: human immunodeficiency virus
MSRA: methicillin-resistant *Staphylococcus aureus*

Figure 1: Source of Methicillin-resistant *S. aureus* (MRSA) Bacteremia at Admission

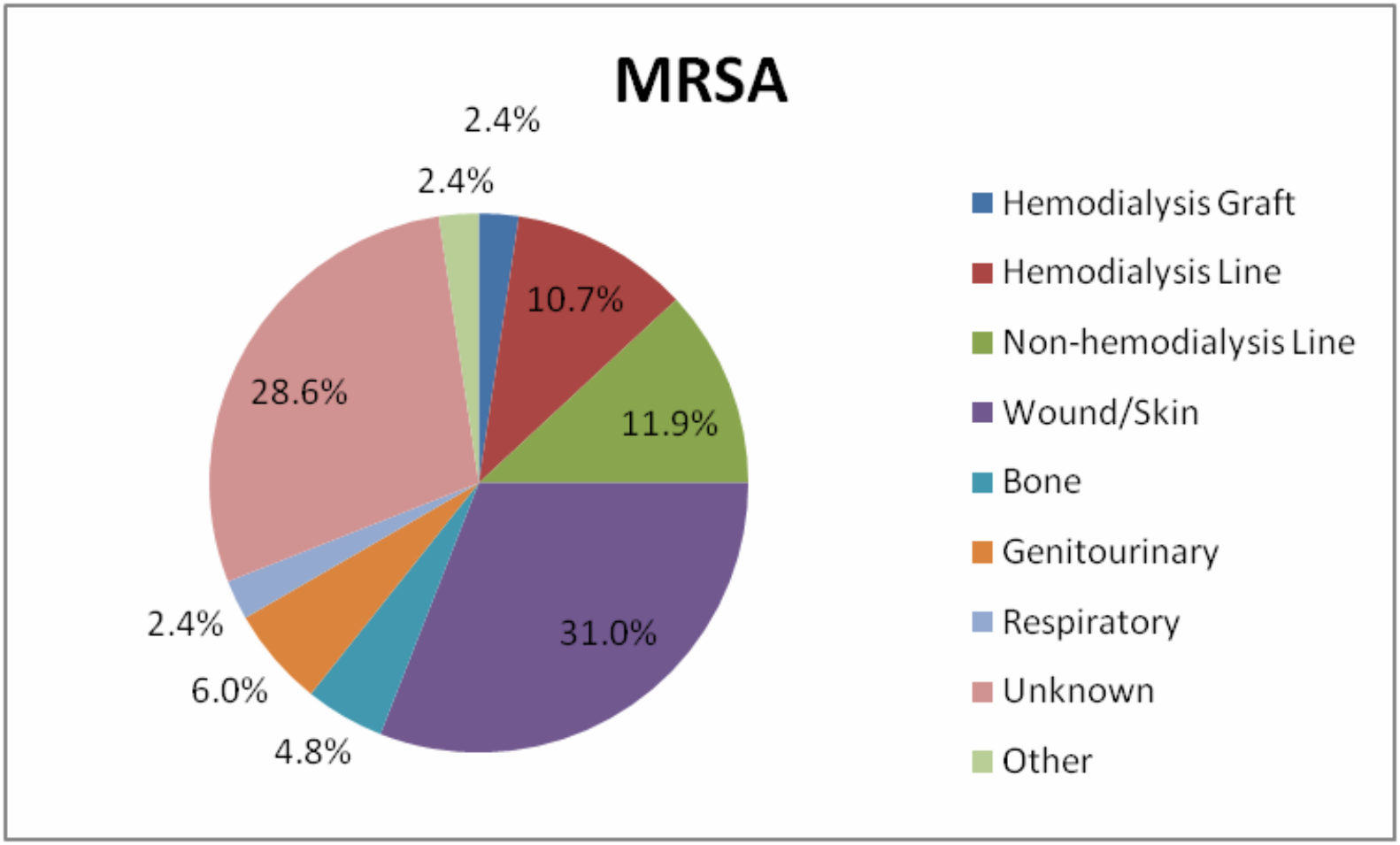

Figure 2: Frequency of Community Onset-Methicillin Resistant *S. aureus* Bacteremia by Quarter, 2005-2008

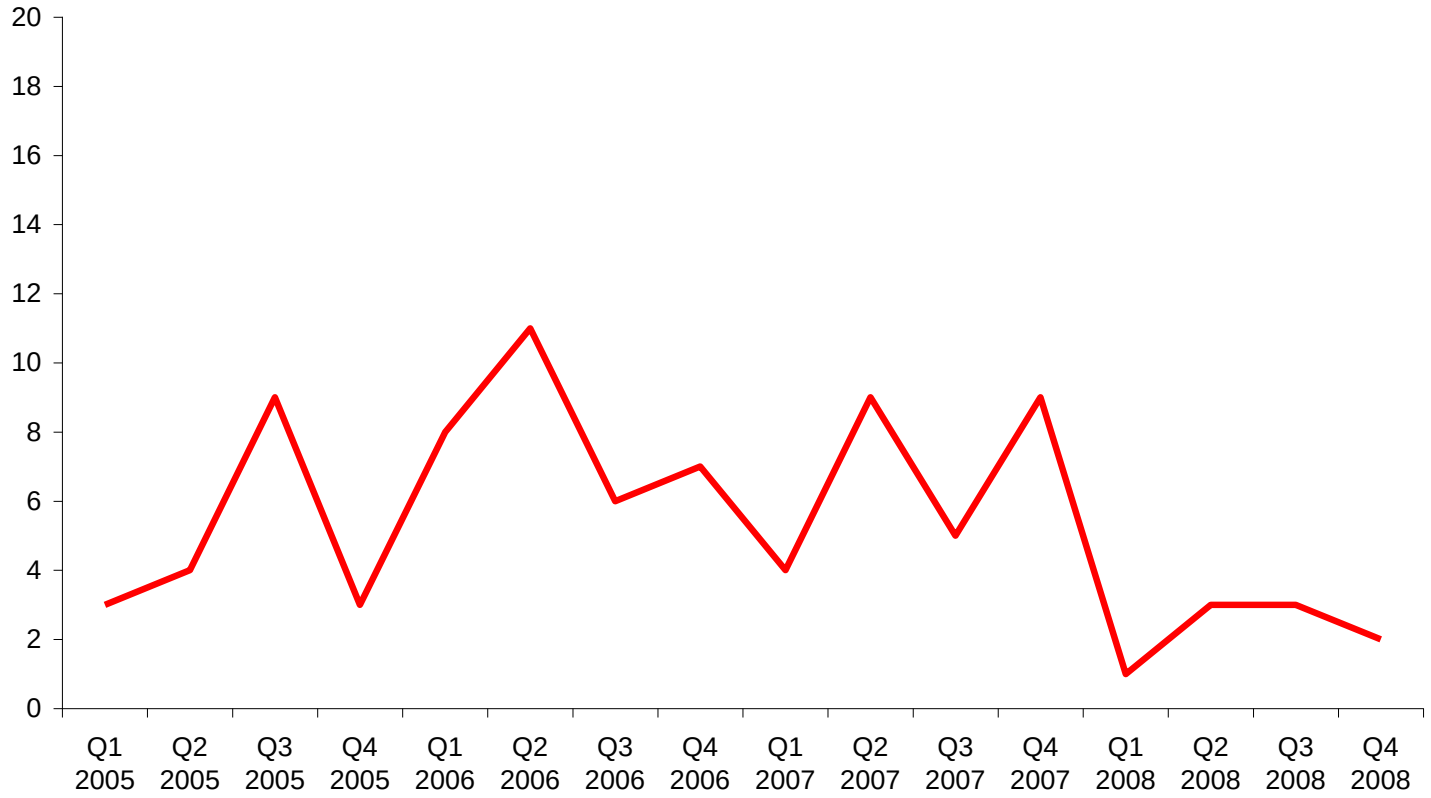

Table 2: Frequency of Selected Characteristics of Patients with Community-Onset *S. aureus* Bacteremia within 90 days

Characteristic	MRSA (n=84)		MSSA (n=58)		p value
	n	%	n	%	
Age in years (mean +/- std dev)	61.0 ± 12.0		63.5 ± 12.1		--
Male	81	94.8	55	96.4	--*
Black race	41	48.8	33	56.9	--
Charlson score >2	43	51.2	29	50	--
Diabetes mellitus	44	52.4	31	53.6	--
Hemodialysis	13	15.5	13	22.4	--
HIV	8	9.5	1	1.7	0.08*
Liver Disease	17	20.4	18	31	--
Antibiotics (90 d)					
Intravenous	45	53.6	17	29.3	<0.01
Oral	66	78.6	31	53.4	<0.01
Prior MRSA (90 d)	12	14.3	0	0	<0.01*
Prior MSSA (90 d)	5	6	3	5.2	--*
Healthcare exposures (90 d)					
Hospitalization	45	53.6	18	31	0.01
Long term care facility	13	15.5	5	8.6	--*
CVC (admission)	22	26.2	13	22.4	--
Clinic visits	81	96.4	56	96.5	--*
ER visits	43	51.2	25	43.1	--
Invasive Procedures	45	53.6	25	43.1	--
Surgery	24	28.6	9	15.5	0.07
Year (2008)	8	9.5	17	29.3	<0.01

*Fisher's exact test
CVC: central venous catheter
MSRA: methicillin-resistant *Staphylococcus aureus*
MSSA: methicillin-sensitive *Staphylococcus aureus*

Figure 3: Number of Community-Onset *S. aureus* Bacteremias by Months Since Last Hospitalization

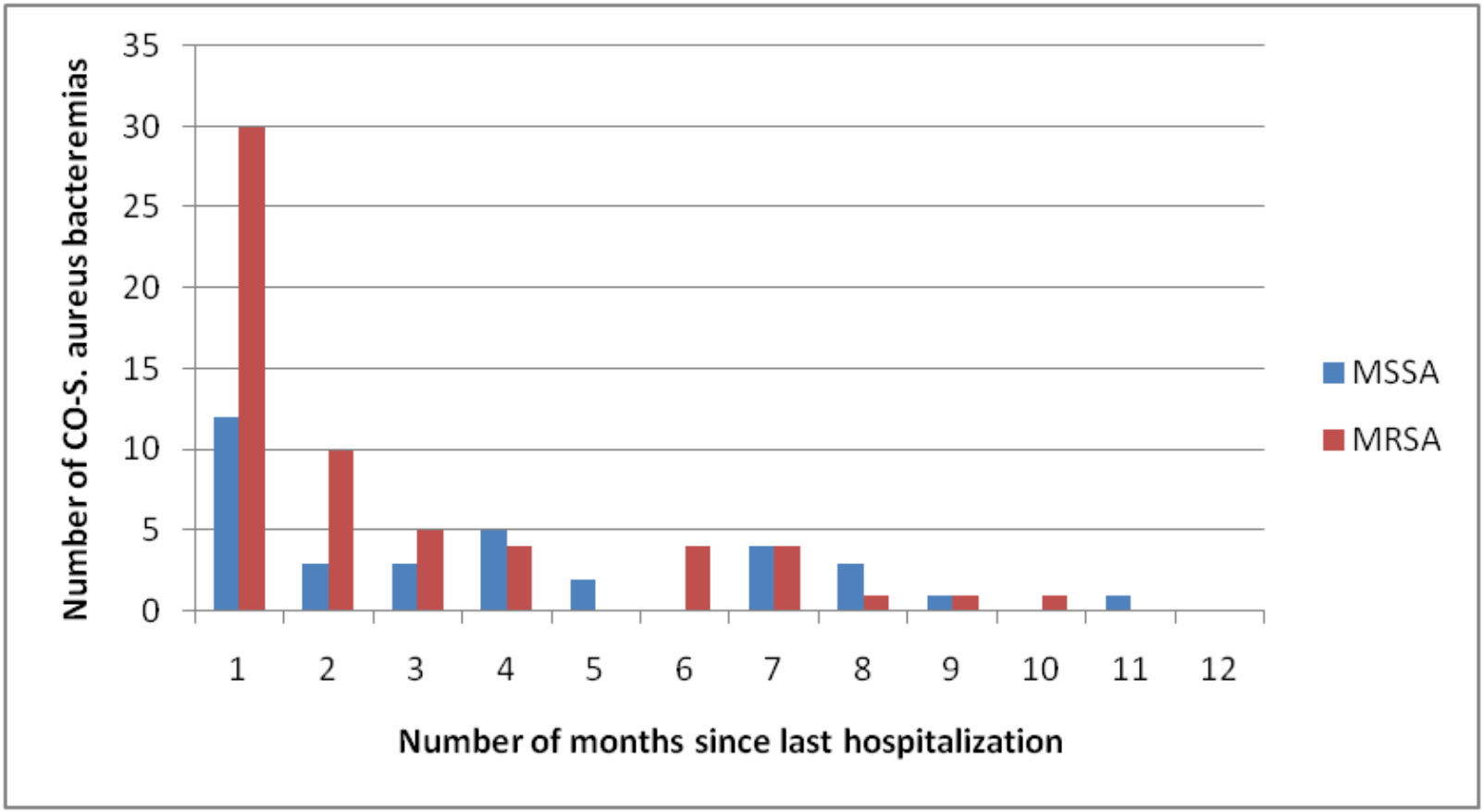

Table 3: Association of Selected Characteristics of Patients with Community-Onset Methicillin-resistant *S. aureus* (MRSA) Bacteremia

Characteristic	OR	95% CI		p value
		LL	UL	
Male gender	1.47	0.29	7.57	--
Black race	0.72	0.37	1.42	--
HIV	6	0.73	49.34	--
Year (2008 vs. 2005-2007)	0.25	0.1	0.63	<0.01
Antibiotics (intravenous) (90 d)	2.78	1.37	5.68	<0.01
Antibiotics (oral) (90 d)	3.19	1.53	6.65	<0.01
Prior MRSA (90 d)	Undefined	--	--	--
Prior MSSA (90 d)	1.16	0.27	5.06	--
Hospitalization (90 d)	2.56	1.27	5.18	<0.01
CVC (admission) (90 d)	1.23	0.56	2.7	--
ER visit (90 d)	1.38	0.71	2.71	--
Invasive procedure (90 d)	1.52	0.78	2.99	--
Long term care facility (90 d)	1.94	0.65	5.78	--
Surgery (90 d)	2.18	0.93	5.11	--

CVC: central venous catheter
ER: emergency room
HIV: human immunodeficiency virus
MSRA: methicillin-resistant *Staphylococcus aureus*
MSSA: methicillin-sensitive *Staphylococcus aureus*

Table 4: Assessment of Interaction of Hospitalization with Other Covariates

Characteristic	Stratum 1 OR	Stratum 2 OR	Mantel-Haenzel OR	95% CI LL	95% CI UL	BD p value
Male gender	--	--	2.56	1.28	5.21	--
Black race	--	--	2.72	1.33	5.53	--
Antibiotics (IV) Yes/No	7.42	0.85	--	--	--	0.01
Antibiotics (oral)	--	--	2.24	1.08	4.63	--
CVC (admission)	--	--	2.65	1.26	5.57	--
ER visit	--	--	2.82	1.24	6.41	--
Procedure	--	--	2.87	1.19	6.89	--
Surgery	--	--	2.23	1.07	4.67	--

Crude OR for Antibiotic (IV)=2.56

CVC: central venous catheter
ER: emergency room
HIV: human immunodeficiency virus

Table 5: Multivariate Analysis of Risk Factors for Methicillin-resistant *S. aureus* (MRSA) Compared to Methicillin-sensitive *S. aureus* Bacteremia: Basic Model

Characteristic	OR	95% CI		p value
		LL	UL	
Antibiotics (oral)	3.82	1.39	10.52	<0.01
Hospitalization in last 90 days	2.80	1.09	7.17	0.03

Tables 6A and 6B: Multivariate Analysis of Risk Factors for Methicillin-resistant *S. aureus* (MRSA) Compared to Methicillin-sensitive *S. aureus* Bacteremia: Basic Model Stratified by IV Antibiotics

IV Antibiotics

Characteristic	OR	95% CI		p value
		LL	UL	
Antibiotics (oral)	1.24	0.21	7.26	--
Hospitalization in last 90 d	5.77	1.44	23.11	0.01

No IV Antibiotics

Characteristic	OR	95% CI		p value
		LL	UL	
Antibiotics (oral)	3.61	0.84	15.52	0.08
Hospitalization in last 90 d	1.69	0.39	7.30	--

Tables 7A and 7B: Multivariate Analysis of Risk Factors for Methicillin-resistant *S. aureus* (MRSA) Compared to Methicillin-sensitive *S. aureus* Bacteremia: Extended Model Stratified by IV Antibiotics

IV Antibiotics

Characteristic	OR	95% CI		p value
		LL	UL	
Antibiotics (oral)	1.59	0.23	11.1	--
Hospitalization in last 90 d	7.67	1.20	49.14	0.03
Hemodialysis	2.37	0.27	20.5	--
CVC (admission)	0.83	0.15	4.77	--
Admission to long term care facility	1.45	0.22	9.59	--
ER visit	1.44	0.26	7.83	--
Surgery	0.81	0.14	4.60	--
Invasive Procedure	0.45	0.07	3.08	--

No IV Antibiotics

Characteristic	OR	95% CI		p value
		LL	UL	
Antibiotics (oral)	3.63	0.45	29.13	--
Hospitalization in last 90 d	6.43	0.32	131.22	--
Hemodialysis	0.39	0.02	7.86	--
CVC (admission)	0.40	0.03	4.87	--
Admission to long term care facility	1.19	0.14	10.18	--
ER visit	0.45	0.03	7.15	--
Surgery	2.68	0.34	20.83	--
Invasive Procedure	0.43	0.05	3.89	--

CVC: central venous catheter
ER: emergency room
HIV: human immunodeficiency virus

Table 8A and 8B: Final Model of Multivariate Analysis of Risk Factors for Methicillin-resistant *S. aureus* (MRSA) Compared to Methicillin-sensitive *S. aureus* Bacteremia, Stratified by IV Antibiotics

IV Antibiotics

Characteristic	OR	95% CI		p value
		LL	UL	
Antibiotics (oral)	1.19	0.20	6.97	--
Hospitalization in last 90 d	6.12	1.50	25.00	0.01
Long term care facility stay	1.81	0.29	11.07	--

No IV Antibiotics

Characteristic	OR	95% CI		p value
		LL	UL	
Antibiotics (oral)	3.42	0.78	14.94	--
Hospitalization in last 90 d	1.72	0.39	7.53	--
Long term care facility stay	1.79	0.24	13.12	--

Table 9A and 9B: Sensitivity analysis excluding patients with prior Methicillin-resistant *S. aureus* (MRSA) of the Final Model of Multivariate Analysis of Risk Factors for MRSA Compared to Methicillin-sensitive *S. aureus* Bacteremia, Stratified by IV Antibiotics

IV Antibiotics

Characteristic	OR	95% CI		p value
		LL	UL	
Antibiotics (oral)	1.23	0.20	7.55	--
Hospitalization in last 90 d	4.37	1.05	18.17	0.04
Long term care facility stay	2.12	0.36	12.58	--

No IV Antibiotics

Characteristic	OR	95% CI		p value
		LL	UL	
Antibiotics (oral)	2.69	0.60	12.08	--
Hospitalization in last 90 d	1.38	0.31	6.14	--
Long term care facility stay	2.10	0.29	15.38	--

Table 10A and 10B: Sensitivity analysis excluding patients with infections in 2008 of the Final Model of Multivariate Analysis of Risk Factors for Methicillin-resistant *S. aureus* (MRSA) Compared to Methicillin-sensitive *S. aureus* Bacteremia, Stratified by IV Antibiotics

IV Antibiotics

Characteristic	OR	95% CI		p value
		LL	UL	
Antibiotics (oral)	0.87	0.10	7.44	--
Hospitalization in last 90 d	14.52	2.41	87.60	<0.01
Long term care facility stay	1.68	0.14	20.93	--

No IV Antibiotics

Characteristic	OR	95% CI		p value
		LL	UL	
Antibiotics (oral)	3.72	0.70	19.73	--
Hospitalization in last 90 d	0.85	0.15	4.98	--
Long term care facility stay	2.37	0.16	35.69	--