Epidemiology of Methicillin-Resistant Staphylococcus Aureus Bloodstream Infections from 2013-2017 at Chiang Mai University: What Changes Occurred from 2007-2011?

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Research article

Keywords: MRSA, bloodstream infections, epidemiology, vancomycin MIC

Posted Date: June 8th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-32103/v1>

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Abstract

Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) is an established pathogen that causes hospital-acquired infections worldwide. Bloodstream infection is associated with significant morbidity and mortality. We conducted a study aimed at describing the epidemiology of MRSA bloodstream infections, to determine the minimal inhibitory concentration (MIC) of the antibiotic vancomycin among MRSA isolates, and to determine the rate and risk factors of mortality.

Methods: A retrospective study was conducted among patients aged ≥ 18 years whose blood culture grew MRSA at Chiang Mai University from January 2013 to December 2017

Results: The annual prevalence of MRSA in *S.aureus* bloodstream infections from 2013 to 2017 were 32.8, 23.1, 26.8, 19.2 and 15.4%, respectively. This prevalence showed a non-significant decrease ($p = 0.086$). Eighty-four patients with 84 episodes of MRSA bloodstream infections were enrolled. Fifty-three patients (63.1%) were male, and the median age was 68.5 years (IQR 56, 79). Fifty-eight patients (69%) had bloodstream infections with other sites of infection: pneumonia (28 episodes, 43.1%), skin and soft tissue infections (16 episodes, 24.6%), osteomyelitis (7 episodes, 10.8%), infective endocarditis (4 episodes, 6.2%), septic arthritis (4 episodes, 6.2%), arterial graft infections (4 episodes, 6.2%), and urinary tract infections (2 episodes, 3.1%). Percentage of patients with vancomycin MICs ≥ 1.5 mg/L were 68.2%, 62.5%, 47.4%, 26.7%, and 75% from 2013 to 2017, respectively. ($p = 0.325$). The mortality rate was 64.3%. There was no significant difference in mortality rate between those infected with MRSA with a MIC of vancomycin < 1.5 and ≥ 1.5 mg/L ($p = 0.172$). Factors associated with mortality included age ≥ 40 years old (OR 11.35; 95% CI: 1.35–95.78, $p = 0.026$), presence of alteration of consciousness (OR 11.19; 95% CI: 2.83–44.18, $p = 0.001$) and concurrent pneumonia (OR 4.44; 95% CI: 1.09–18.14, $p = 0.038$).

Conclusions: Methicillin-resistance among *Staphylococcus aureus* bloodstream infections showed a non-significant decrease of 50%, from 32.88% and 15.4%, between 2013 and 2017. Concurrent infection with pneumonia increased mortality. Although the vancomycin MIC was unchanged from 2013 to 2017, the mean MICs were > 1.0 mg/L. Careful monitoring of vancomycin MIC creep is crucial for the selection of the appropriate antibiotic dosage to prevent treatment failure.

Background

Methicillin-resistant *Staphylococcus aureus* (MRSA) is an established pathogen that causes hospital-acquired infections worldwide.[1] MRSA bloodstream infection (BSI) is associated with significant morbidity and mortality.[2] The prevalence rate of methicillin resistance among *S.aureus* infections varies widely depending upon the study site and the year of the study. The SENTRY antimicrobial surveillance program collected 191,460 *S. aureus* isolates from 427 centers globally.[3] From 1997 to 2016, the prevalence of MRSA among *S. aureus* ranged between 26.8% in Europe and 47.0% in North America. In the Asia-Pacific area, which includes Thailand, the prevalence was 39.6%. Among hospital-acquired *S.aureus* BSI, the prevalence of MRSA ranged from 37.8–45.3%. The ANSORP study group collected the

isolates from 2004 to 2006 in Asian countries and found that the prevalence of MRSA among *S.aureus* isolates was highest in Sri Lanka (86.5%) and lowest in India (22.6%).[4] In Thailand, the prevalence of MRSA among *S.aureus* isolates from university hospitals from 2005–2006 was 57%, [4] and from 2012–2015 was 46.0%.[5] A study from northeastern Thailand reported the prevalence of MRSA among *S. aureus* BSI during 2006–2007 was 28%.[6] A prevalence of MRSA among *S.aureus* BSI of 23–43% during 2007–2011 from northern Thailand was also reported.[7]

Vancomycin is the mainstay treatment for MRSA infection. However, infections caused by MRSA with reduced susceptibility to vancomycin have been reported including some cases in Thailand.[8–12] In addition, there have been increasing reports about patients who had treatment failure from vancomycin, despite their vancomycin MIC being ≤ 2 mg/L. [13–15] The increase in vancomycin MIC but within the susceptible range of MRSA is called the creep phenomenon.[16] Patients with MRSA BSIs with an elevated vancomycin MIC (≥ 1.5 mg/L) had poor clinical outcomes i.e. longer durations of bacteremia, higher recurrence rate of MRSA bacteremia after vancomycin discontinuation, longer hospital stays, and increased mortality. [17–19] In addition, the number of patients infected with MRSA with a vancomycin MIC ≤ 0.5 mg/L was associated with treatment success if compared with those infected with strains of vancomycin MIC of 1–2 mg/L.[20]

We conducted this study along the same lines as the one conducted from 2007–2011 which aimed to describe the epidemiology, characteristics, mortality rate, and risk factors of death among patients who had MRSA BSIs. In addition, we also determine vancomycin MIC among MRSA isolates from hemoculture. Vancomycin MIC was routinely performed for blood cultures growing MRSA in our hospital from 2012.

Methods

A retrospective study was conducted at the Maharaj Nakorn Chiang Mai hospital, a 1400-bed, university affiliated hospital in northern Thailand. Adult inpatients aged ≥ 18 years and had MRSA grown from blood culture from January 2013 to December 2017 were enrolled. Demographic and clinical characteristics, laboratory information, and microbiological data were collected.

Microbiological methods

Bacterial identification and antimicrobial susceptibility testing were performed at the Microbiology unit, Diagnostic laboratory, Maharaj Nakorn Chiang Mai hospital. *S. aureus* was identified by conventional biochemical tests. All *S. aureus* isolates were tested against 5 antibiotics including oxacillin (using cefoxitin as a surrogate drug), vancomycin, trimethoprim-sulfamethoxazole, erythromycin and clindamycin by disk diffusion method following the Clinical and Laboratory Standards Institute (CLSI) guidelines, M02-A11 [21] and M02-A12.[22] The disk diffusion results were interpreted according to the breakpoints stated in the CLSI guidelines, M-100 series.[22] A further minimal inhibitory concentration (MIC) test of vancomycin was performed among the MRSA samples isolated from blood cultures. MIC is

the lowest concentration of a chemical which prevents visible growth of a bacterium. According to the CLSI, MRSA can be categorized into 3 groups: MIC $\leq$ 2 mg/L refers to vancomycin-susceptible *S.aureus*; MIC 4–8 mg/L refers to vancomycin-intermediate resistant *S. aureus* (VISA), and MIC $\geq$ 16 mg/L refers to vancomycin-resistant *S.aureus* (VRSA).[22]

Statistical analysis

Data were presented as numbers (%), means and standard deviation (SD), or medians and interquartile ranges (IQR) as appropriate. Characteristics between groups were compared using the Student's t-test, Mann-Whitney *U* test, Chi-square test or Fisher's exact test as appropriate. Factors associated with mortality were analyzed using a univariate logistic regression model. Variables with a p-value < 0.10 from the univariate analysis were then tested in a multivariate logistic regression model using a backward stepwise procedure. A two-sided test with a p-value of < 0.05 was used to determine statistical significance. All statistical analyses were performed using Stata statistical software version 10.0 (Stata Statistical Software: Release 10.0, Stata Corporation, College Station, TX).

This study was approved by the Faculty of Medicine Ethical Committee, approval number MED-2561-05488.

Results

The prevalence of MRSA among *S.aureus* BSIs from 2013 to 2017 were 32.8, 23.1, 26.8, 19.2 and 15.4%, respectively (*p*-value for trend = 0.086). Eighty-four patients with MRSA BSIs were enrolled; the numbers of patient in 2013, 2014, 2015, 2016 and 2017 were 22, 16, 19, 15, and 12, respectively.

Demographic data

Fifty-three patients (63.1%) were male. The median age was 68.5 years (IQR 56, 79). Twenty-four patients (28.6%) were admitted to the intensive care unit (ICU). The details of hospital units is shown in Table 1. Seventy-two patients (85.7%) had underlying diseases. The 5 most common underlying diseases were, in decreasing order: hypertension, chronic kidney disease, diabetic mellitus, dyslipidemia and malignancy (Table 1). Patients who had previous hospitalization within 3 months numbered 45 (53.6%), and prior antibiotic use within 3 months were 73 patients (86.9%).

Table 1
Demographic characteristic of patients who had MRSA
bloodstream infections

Characteristics	Number (%) N = 84
Male	53 (63.1)
Age in years (median, IQR)	68.5 (56, 79)
Presence of underlying disease	72 (85.7)
- Hypertension	32 (38.1)
- Chronic kidney disease	31 (36.9)
- Diabetes mellitus	16 (19.3)
- Dyslipidemia	14 (16.7)
- Malignancy	14 (16.7)
- Chronic obstructive pulmonary disease	8 (9.5)
- Cerebrovascular accident	8 (9.5)
- Valvular heart disease	6 (7.1)
- Dilated cardiomyopathy	5 (6.0)
- Coronary artery disease	5 (6.0)
- History of surgery of aortic arterial aneurysm	4 (4.8)
- Bronchiectasis	1 (1.2)
- Human immunodeficiency virus	1 (1.2)
Prior hospitalization within 3 months	45 (53.6)
Prior antibiotic within 3 months	73 (86.9)
Beta-lactams antibiotics:	
- Cloxacillin	7 (8.3)
- Ampicillin	3 (3.6)
- Amoxicillin/clavulanate	4 (4.8)
- Piperacillin/tazobactam	25 (29.8)
- Cefazolin	3 (3.6)
- Ceftriaxone	23 (27.4)

Characteristics	Number (%)
	N = 84
- Ceftazidime	6 (7.1)
- Cefoperazone/sulbactam	2 (2.4)
- Ertapenem	7 (8.3)
- Imipenem/cilastatin	5 (6.0)
- Meropenem	37 (44.1)
Others:	
- Azithromycin	7 (8.3)
- Ciprofloxacin	14 (16.7)
- Clindamycin	11 (13.1)
- Colistin	19 (22.6)
- Fosfomycin	2 (2.4)
- Levofloxacin	1 (1.2)
- Metronidazole	2 (2.4)
- Trimethoprim/sulfamethoxazole	1 (1.2)
- Vancomycin	12 (14.3)
Unit of admission	
- General internal medicine	36 (42.9)
- Intensive care of internal medicine	15 (17.9)
- General surgery	20 (23.8)
- Intensive care of surgery	8 (9.5)
- General orthopedics	4 (4.8)
- Intensive care of orthopedics	1 (1.2)

Clinical characteristics

Fifty-eight patients (69%) had bloodstream infections with concurrent other sites of infection: pneumonia 28 episodes (43.1%), skin and soft tissue infections 16 episodes (24.6%), osteomyelitis 7 episodes (10.8%), infective endocarditis 4 episodes (6.2%), septic arthritis 4 episodes (6.2%), arterial graft infections 4 episodes (6.2%) and urinary tract infections 2 episodes (3.1%). Sixty-five patients (77.4%) had medical devices inserted: central venous catheter 45 patients (53.6%), urinary catheter 43 patients

(51.2%), nasogastric tube 40 patients (47.6%), and endotracheal tube 39 patients (46.4%). Sixty-one patients (72.6%) had a body temperature ≥ 38.0 °C, and 10 patients (11.9%) had blood pressure < 90/60 mm.Hg. Forty-eight patients (57.1%) had alteration of consciousness (Table 2)

Table 2
Clinical characteristics and laboratory data of patients infected with MRSA
bloodstream infections

Characteristics	Values (N = 84)
Presence of medical devices	65 (77.4)
- Central venous catheter	45 (53.6)
- Urinary catheter	43 (51.2)
- Nasogastric tube	40 (47.6)
- Endotracheal tube	39 (46.6)
Signs and symptoms	
- Alteration of consciousness	48 (57.1)
- Body temperature ≥ 38.0 °C	61 (72.6)
- Blood pressure < 90/60 mm.Hg	10 (11.9)
- Tachycardia (heart rate ≥ 120 beat/minute)	26 (31.0)
- Tachypnea (respiratory rate > 20/ minute)	55 (65.5)
Site of infections:	
- Primary blood stream infection (BSI)	26 (31.0)
- BSI with pneumonia	28 (33.3)
- BSI with skin and soft tissue infection	16 (19.1)
- BSI with osteomyelitis	7 (8.3)
- BSI with infective endocarditis	4 (4.8)
- BSI with septic arthritis	4 (4.8)
- BSI with arterial graft infection	4 (4.8)
- BSI with urinary tract infection	2 (2.4)
Laboratory findings:	
- Hemoglobin (g/dL)	9.1 $\pm$ 1.5
- White blood cell count (cell/cu.mm.)	11,850 (7,935, 18,250)
- Neutrophil (%)	84.8 (78.5, 89.7)

Data are presented as number (%), mean ($\pm$ SD), or median (IQR) as appropriate

Characteristics	Values (N = 84)
- Lymphocyte (%)	7.3 (4.2, 12.2)
- Platelet (x1000/cu.mm.)	207 (110.5, 272)
- Creatinine (mg/dl)	2.1 (0.9, 4.4)
- Albumin (mg/dl)	2.5 ± 0.6
- Aspartate aminotransferase (IU/L)	32 (21, 74)
- Vancomycin MIC (mg/L)	1.3 ± 0.4
Data are presented as number (%), mean (± SD), or median (IQR) as appropriate	

Drug susceptibility testing

All isolates were susceptible to vancomycin according to CLSI guidelines. Sixty-three isolates (75%) were susceptible to trimethoprim/sulfamethoxazole, 3 isolates (3.6%) susceptible to clindamycin, and 4 isolates (4%) were susceptible to erythromycin.

Vancomycin MIC

Three patients had missing vancomycin MIC, 1 in each of the years 2013, 2015, and 2017. That means vancomycin MICs from 2013 to 2017 were 1.45, 1.47, 1.24, 1.02 and 1.50 mg/L, respectively. Percentage of patients with vancomycin MICs ≥ 1.5 mg/L were 68.2%, 62.5%, 47.4%, 26.7%, and 75% from 2013 to 2017, respectively ($p = 0.325$) (Fig. 1).

Treatment and outcome

Seventy-nine patients received anti-MRSA treatment; 72 patients (85.7%) received vancomycin, 5 patients (6.0%) received linezolid, and 2 patients (2.4%) received fosfomycin. The median time from positive blood culture to receipt of appropriate antibiotics was 1 day (IQR 0, 3). The other 5 patients did not receive anti-MRSA treatment and died.

Fifty-four patients died giving a mortality rate of 64.3%. The patients who died were more likely to be older, had had prior use of piperacillin/tazobactam within 3 months, presence of alteration of consciousness, tachypnea, presence of medical devices, had concurrent pneumonia, and lower platelet count. Patients who survived were more likely to have an underlying condition of chronic kidney disease. (Tables 3 and 4)

Table 3
Comparisons of demographic characteristics between patients who survived and who died

Variables	Patients who survived N (%) (N = 30)	Patients who died N (%) (N = 54)	P-values
Male	19 (63.3)	19 (63.3)	0.973
Age in years (median, IQR)	63 (54,72)	74.5 (61,83)	0.004
Presence of underlying diseases:	25 (83.3)	47 (87.0)	0.748
- Hypertension	11 (36.7)	21 (38.9)	0.841
- Chronic kidney disease	16 (53.3)	15 (27.8)	0.020
- Diabetes mellitus	9 (30.0)	7 (13.2)	0.062
- Malignancy	4 (13.3)	10 (18.5)	0.761
- Chronic obstructive pulmonary diseases	2 (6.7)	6 (11.1)	0.705
- Cerebrovascular accident	3 (10.0)	5 (9.3)	1.000
- Valvular heart disease	1 (3.3)	5 (9.3)	0.414
- Dilated cardiomyopathy	1 (3.3)	4 (7.4)	0.651
- Coronary artery disease	1 (3.3)	4 (7.4)	0.651
- History of surgery abdominal aortic aneurysm	2 (6.7)	2 (3.7)	0.614
Prior hospitalization within 3 months	15 (50.0)	30 (55.6)	0.625
Prior antibiotic within 3 months	25 (83.3)	48 (88.9)	0.511
Beta-lactam antibiotics:			
- Cloxacillin	4 (13.3)	3 (5.6)	0.242
- Amoxicillin/clavulanate	1 (3.3)	3 (5.6)	1.000
- Piperacillin/tazobactam	3 (10.0)	22 (40.7)	0.003
- Cefazolin	2 (6.7)	1 (1.9)	0.289
- Ceftriaxone	6 (20.0)	17 (31.5)	0.258
- Ceftazidime	3 (10.0)	3 (5.6)	0.662
- Ertapenem	4 (13.3)	3 (5.6)	0.242
- Imipenem/cilastatin	2 (6.7)	7 (13.0)	0.480

Variables	Patients who survived N (%) (N = 30)	Patients who died N (%) (N = 54)	P-values
- Meropenem	11 (36.7)	26 (48.2)	0.310
Others:			
- Azithromycin	2 (6.7)	5 (9.3)	1.000
- Ciprofloxacin	7 (23.3)	7 (13.0)	0.222
- Clindamycin	5 (16.7)	6 (11.1)	0.511
- Colistin	3 (10.0)	16 (29.6)	0.056
- Metronidazole	2 (6.7)	7 (13.0)	0.480
- Vancomycin	4 (13.3)	8 (14.8)	1.000
Unit of admission:			
- General internal medicine	13 (43.3)	23 (42.6)	0.948
- Intensive care of internal medicine	3 (10.0)	12 (22.2)	0.236
- General surgery	6 (20.0)	14 (25.9)	0.541
- Intensive care of surgery	4 (13.3)	4 (7.4)	0.448
- General orthopedics	3 (10.0)	1 (1.9)	0.128
- Intensive care of orthopedics	1 (3.3)	0 (0.0)	0.357

Table 4

Comparisons of clinical characteristics between patients who survived and who and those who died

Variables	Patients who survived (N = 30)	Patients who died (N = 54)	P-values
Presence of medical devices	20 (66.7)	45 (83.3)	0.080
- Central venous catheter	14 (46.7)	31 (57.4)	0.344
- Urinary catheter	8 (26.7)	35 (64.8)	0.001
- Nasogastric tube	6 (20.0)	34 (63.0)	< 0.001
- Endotracheal tube	6 (20.0)	33 (61.1)	< 0.001
Sign and symptoms			
- Alteration of consciousness	8 (26.7)	40 (74.1)	< 0.001
- Body temperature ≥ 38.0 °C	23 (76.7)	38 (70.4)	0.616
- Blood pressure < 90/60 mm.Hg	2 (6.7)	8 (14.8)	0.483
- Tachycardia (heart rate ≥ 120 beat/minute)	8 (26.7)	18 (33.3)	0.626
- Tachypnea (respiratory rate > 20/ minute)	16 (53.3)	39 (72.2)	0.097
Bloodstream infections without other site of infections	14 (46.7)	12 (22.2)	0.020
Concurrent site of infections			
- Pneumonia	3 (10.0)	25 (46.3)	0.001
- Skin and soft tissue infection	6 (20.0)	10 (18.5)	0.868
- Osteomyelitis	5 (16.7)	2 (3.7)	0.092
- Infective endocarditis	0 (0.0)	4 (7.4)	0.292
- Septic arthritis	2 (6.7)	2 (3.7)	0.614
- Arterial graft infection	2 (6.7)	2 (3.7)	0.614
- Urinary tract infection	0 (0.0)	2 (3.7)	0.535
Laboratory findings:			
- Hemoglobin (g/dL)	9.1 $\pm$ 1.6	9.1 $\pm$ 1.5	0.978

Variables	Patients who survived (N = 30)	Patients who died (N = 54)	P-values
- White blood cell count (cells/cu.mm)	10,950 (7,700, 12,800)	12,355 (8,100,19,100)	0.170
- Neutrophil (%)	83.3 (78.8,88.2)	87.1 (78.6,90.0)	0.130
- Platelet (x1000/cu.mm)	234.5 (189, 306)	156.5 (72, 266)	0.024
- Creatinine (mg/dL)	2.0 (0.7,6.6)	2.1 (0.9,3.5)	0.493
- Albumin (mg/dL)	2.6 ± 0.5	2.5 ± 0.6	0.477
- Alanine aminotransferase (IU/L)	6 (12, 27)	21 (13, 58)	0.186
- Vancomycin MIC (mg/L)	1.5 ± 0.4	1.3 ± 0.4	0.085

The multivariate analysis found that factors associated with mortality were: age ≥ 40 years old (OR 11.35; 95% CI: 1.35–95.78, $p = 0.026$), presence of alteration of consciousness (OR 11.19; 95% CI: 2.83–44.18, $p = 0.001$) and concurrent pneumonia (OR 4.44; 95% CI: 1.09–18.14, $p = 0.038$). Patients with chronic kidney disease were associated with survival. There was no significant difference in mortality rate between those infected with MRSA with vancomycin MIC ≤ 1 and > 1 mg/L ($p = 0.617$).

Discussion

This study demonstrated that the prevalence of MRSA among *S.aureus* BSIs was non-significantly decreasing over this 5-year period, from 33–15%. This finding is in contrast with our study conducted between 2007 and 2011, in which there was an increasing prevalence, doubling from 23–43%. [7] The SENTRY study reported a prevalence of 37.8% in the period 1997–2000, reaching a peak of 45.3% in 2005–2008, slightly declining to 40.0% from 2013–2016.[3] The surveillance of antimicrobial resistance in Europe in 2018 showed a large difference in MRSA percentages ranging from 0–43%, giving an average rate of 16.4% in 2018. Almost one-third of European countries reported a significant decrease in the resistance rate from 2015–2018. [23] The decreasing trend in many countries may be attributed to the new technology enabling early detection of MRSA, leading to prompt initiation of appropriate antibiotics to reduce colonization pressure and improvement in infection control measures.

Demographic and clinical characteristics are comparable to the previous reports. The majority of patients had underlying diseases, had prior exposure to antibiotics within 3 months, and had medical devices inserted. Seventy percent of patients had concurrent other infections; 33% of patients had pneumonia and 19% of patients had skin and soft tissue infection. [6, 7, 24]. All clinical isolates were sensitive to vancomycin according to vancomycin MIC.

Vancomycin is a life-saving medication, and has been the mainstay of treatment for MRSA infections for several years. Although new medication i.e. linezolid, daptomycin, and ceftaroline is available, [25] they are not widely accessible for the majority of patients in Thailand, mainly due to high cost. Vancomycin has a narrow therapeutic index, high levels can cause toxicity and low levels can result in treatment failure. [26] Therefore, drug level must be monitored for patients receiving vancomycin. A level of 15–20 mg/L is required for treatment success of BSIs.[26, 27] The pharmacokinetics (Pk)/pharmacodynamics (Pd) parameter of vancomycin, which is the area under the curve (AUC) above the minimal inhibitory concentration (MIC) of > 400 is correlated with good clinical outcome.[27] However, in the era of vancomycin MIC creeps, higher drug levels may be required to achieve that Pk/Pd parameter. In the past, vancomycin MICs were mostly < 0.5 mg/L.[28, 29] however, many reports demonstrated that vancomycin MICs are increasing.[16, 28–30] A study in the US, reported a vancomycin MIC ≥ 1 mg/L from 2000–2008. [30] In China, the percentages of vancomycin MIC = 1 mg/L increased from 37.0% in 2006 to 75.7% in 2010. (25) In this current study, vancomycin MIC for each year was mostly ≥ 1 mg/dL. Sixteen patients (19.7%) had vancomycin MIC = 2 mg/L. There are conflicting data with regard to the association between treatment failure and an MIC of 1.5 mg/L or greater. [18, 19, 31, 32] This study demonstrated no association between mortality and an MIC of 1.5 mg/L or greater. Given a vancomycin MIC of ≤ 1.5 mg/L, vancomycin is still a mainstay of treatment for MRSA infection in our hospital. However, as some strains had an MIC of 2.0 mg/L, clinicians should be aware of MIC creep and monitor the position continuously.

A systematic review and meta-analysis reported mortality rates of MRSA BSI, ranging from 14.2–41.8% between 2006 and 2011.[18] Our previous study which was conducted between 2007 and 2011 reported a mortality of 53.1%. [7] Mortality rate among those who had vancomycin MIC < 1.5 mg/L ranged from 9 and 39% and those who had vancomycin MIC ≥ 1.5 mg/L ranged from 5 and 66%. [18] Not all studies demonstrated a higher mortality rate among those who had MIC ≥ 1.5 mg/L.

Factors associated with death included older age, presence of alteration of consciousness and concurrent pneumonia. Aging is associated with low immunity, [33] alteration of consciousness may represent signs of sepsis, [34, 35] and concurrent pneumonia may be associated with prolonged hospitalization, frequent use of medical devices and broad-spectrum antimicrobials, which may directly or indirectly lead to fatal outcome. In addition to those factors, other studies also reported that those receiving corticosteroids, requiring mechanical ventilation, had sepsis or septic shock, and failure to receive anti-MRSA antibiotics within 24 hours of MRSA identification all had a higher incidence of fatality. [36–38] Chronic kidney disease reduced the risk of mortality as these patients, particularly those receiving renal replacement therapy, are acknowledged to be at risk of infection caused by MRSA or coagulase-negative staphylococci and are given early anti-MRSA therapy as a component of empirical antimicrobials.

What changed from the study carried out from 2007–2011? First, the number of cases declined and the prevalence of MRSA among *S. aureus* BSI decreased. Second, the clinical characteristics in both studies were somewhat similar i.e. majority of patients had underlying diseases, and medical devices insertion.

Most common concurrent infections were pneumonia and skin and soft tissue infections. Third, with data available, the mean vancomycin MIC were ≥ 1 mg/L. Fifty-six percent of isolates had vancomycin MIC ≥ 1.5 mg/L. Fourth, the mortality rate was higher in the current study, which might be explained by the fact that more patients in the current study had underlying diseases (however, we could not directly test for statistically significant difference). Finally, risk factors of death were somewhat similar.

This study had several limitations. First, due to it being a retrospective study, some data may be missing and lead to misinterpretation of the results, e.g. the leading cause of death might be due to MRSA infection itself or from other causes. Second, the number of patients recruited was small; therefore, factors associated with death may not have been detected.

Conclusions

MRSA among *S.aureus* BSIs shows a non-significant decrease by half from 2013 and 2017. Concurrent bloodstream infection and pneumonia increased mortality. Although the vancomycin MIC was unchanged from 2013 to 2017, more than half of the patients had vancomycin MIC ≥ 1.5 mg/L. Careful monitoring of vancomycin MIC creep is crucial for selection of appropriate antibiotic therapy to prevent treatment failure.

List Of Abbreviations

BSI, bloodstream infection; CLSI, Clinical and Laboratory Standards Institute; IQR, interquartile range; mg/L, milligram/ liter; MRSA, methicillin-resistant *Staphylococcus aureus*; MIC, minimal inhibitory concentration; OR, odds ratio; VRSA, vancomycin-resistant *Staphylococcus aureus*; VISA, vancomycin-intermediate resistant *Staphylococcus aureus*; SD, standard deviation

Declarations

Ethics approval and consent to participate:

This study was approved by the Faculty of Medicine Ethical Committee, approval number MED-2561-05488. Written informed consent was not obtained as we retrospectively collected the existing data.

Consent for publication:

Not applicable

Availability of data and materials:

Data will not be shared as the local IRB has no policy to share the data without prior permission.

Competing interests:

The authors declare that they have no competing interests.

Funding:

None

Authors' contributions:

KK participated in data collection, data analysis, data interpretation, and drafted the manuscript. SY participated in data analysis and data interpretation. PK participated in data collection. RC participated in the trial design, data analysis, data interpretation, and drafted the manuscript. All authors read and approved the final manuscript.

Acknowledgements:

The authors would like to thank Mrs. Joan Elizabeth Peagamresearch administration section, Faculty of Medicine, Chiang Mai University for their provision of a native English proofreader.

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Figures

Figure 1

Distribution of vancomycin MIC by calendar year