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Research paper

Methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia: Correlations between clinical, phenotypic, genotypic characteristics and mortality in a tertiary teaching hospital in Malaysia

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ABSTRACT

Methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia is a serious infection that can result in significant morbidity and mortality. A retrospective cohort study was conducted to determine the predictors of mortality in patient with MRSA bacteremia correlating with clinical, phenotypic and genotypic characteristics of the relevant strains. Most of the bacteremia cases were healthcare-associated ($P < 0.0001$). Older age ($P < 0.0001$) and comorbidities (diabetes mellitus, hypertension and chronic kidney disease) were identified as the risk factors for MRSA bacteremia. All the strains were sensitive to vancomycin. Most MRSA strains causing bacteremia belonged to SCC*mec* type III-ST239 and exhibited pulsotype H. According to the multivariate analysis, age ≥ 60 years old ($P = 0.022$), female gender ($P = 0.0003$), pneumonia ($P = 0.011$) as source of infection as well as high APACHE II, Charlson comorbidity Index and Pitt's bacteremia scores were significantly associated with patient's mortality. There were emergence of MRSA clones such as SCC*mec* type I-ST152, SCC*mec* type V-ST45 and SCC*mec* type V-ST951 that was discovered for the first time in Malaysia. To our knowledge, this is the first study correlating the clinical, phenotypic and genotypic characteristics of patients with MRSA bacteremia as well as determining the risk factors for mortality in Malaysian hospital.

1. Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia is of major concerns worldwide due to its high incidence rates (Cuervo et al., 2015). In 2016, the percentage of invasive MRSA isolates in Europe ranged from 1.2% in the Netherlands to 50.5% in Romania, with a population-weighted mean of 13.7%. Despite the decreasing MRSA trends during the period 2013 to 2016 in Europe, 10 out of the 30 European Union countries still reported MRSA percentages above 25% (European Centre for Disease Prevention and Control, 2017). In Taiwan, the MRSA bacteremia rates remained above 55% from 2000 to 2010 (Chen and Huang, 2014). MRSA bacteremia is also significantly associated with substantial morbidity and mortality (Chong et al., 2015). The mortality rate for patients with MRSA bacteremia is 20 to 50% (MRSA Survivors Network, 2003). In a study in Canada, MRSA bacteremia patients were reported to have a higher fatality rate (39%) compared to those of methicillin-sensitive *Staphylococcus aureus* (MSSA) (24%) (Laupland et al., 2008).

According to Weigelt (2010), the risk factors for MRSA bacteremia are increased age, male gender, immunosuppression, presence of catheter, past history of MRSA infection, severe underlying disease, intravenous drug user, recent hospitalization and previous antibiotic exposure. In a study done by Pastagia et al. (2012), the important predictors for mortality in MRSA bacteremia include older age, patients with liver cirrhosis and renal insufficiency, residence in a nursing home before hospitalization and intensive care unit (ICU) patients.

In Malaysia, Ahmad et al. (2010) reported that MRSA strains accounted for about 21% of nosocomial bacteremia. However, little is known about the risk factors for mortality in MRSA bacteremia due to the lack of study correlating clinical, phenotypic and molecular data with patient's clinical outcome. Therefore, the objectives of this study were to study the clinical, phenotypic and genotypic characteristics of MRSA strains and to investigate the risk factors associated with mortality in patients with MRSA bacteremia.

2. Materials and methods

2.1. Study design

This retrospective cohort study was conducted at the University

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Table 1
Demographics, clinical, phenotypic and genotypic characteristics of MRSA bacteremia.[a]

	Total *n* = 67 (%)	*P* value[†]	Female *n* = 28	Male *n* = 38	*P* value[†]
Age, years (mean ± SD)	62.38 ± 16.93		68.21 ± 13.82	58.08 ± 17.87	**0.012**
< 60 years old	47.35 ± 10.35	< **0.0001**			
≥60 years old	75.69 ± 8.08				
Not known					
Gender					
Female	28 (41.8)	0.119			
Male	38 (56.7)				
Not known	1 (1.5)				
Co-morbidities					
Diabetes mellitus	33 (49.3)		15 (53.6)	18 (47.4)	0.804
Hypertension	34 (50.7)		16 (57.1)	18 (47.4)	0.465
Chronic kidney disease	35 (52.2)		15 (53.6)	20 (52.6)	1.000
Cancer	10 (14.9)		4 (14.3)	6 (15.8)	1.000
Cerebrovascular injury	17 (25.4)		8 (28.6)	9 (23.7)	0.778
Liver disease	3 (4.5)		2 (7.1)	1 (2.6)	0.569
Respiratory disease	23 (34.3)		10 (35.7)	13 (34.2)	1.000
Cardiovascular disease	10 (14.9)		4 (14.3)	6 (15.8)	1.000
Gastrointestinal disease	3 (4.5)		1 (3.6)	2 (5.3)	1.000
Autoimmune disease	2 (2.9)		2 (7.1)	0 (0)	0.176
Bone and joint disorder	4 (5.9)		1 (3.6)	3 (7.9)	0.631
Endocrine disorder	1 (1.5)		1 (3.6)	0 (0)	0.424
Blood disorder	10 (14.9)		6 (21.4)	4 (10.5)	0.302
HIV	1 (1.5)		0 (0)	1 (2.6)	1.000
Skin disease	1 (1.5)		1 (3.6)	0 (0)	0.424
Not known	1 (1.5)				
Sources of bacteremia					
Primary bacteremia	15 (22.4)		5 (17.9)	10 (26.3)	0.555
Catheter-related bloodstream infection	23 (34.3)		9 (32.1)	14 (36.8)	0.796
Skin and soft tissue infection	6 (8.9)		2 (7.1)	4 (10.5)	0.696
Pneumonia	17 (25.4)		9 (32.1)	8 (21.1)	0.396
Surgical site infection	3 (4.5)		2 (7.1)	1 (2.6)	0.569
Implant-related infection	4 (5.9)		1 (3.6)	3 (7.9)	0.631
Prosthetic valve endocarditis	1 (1.5)		1 (3.6)	0 (0)	0.424
Septic arthritis	1 (1.5)		1 (3.6)	0 (0)	0.424
Not known	1 (1.5)				
SCC*mec* types					
SCC*mec* I	1 (1.5)		1 (3.6)	0 (0)	0.424
SCC*mec* II	0 (0)		0 (0)	0 (0)	
SCC*mec* III	37 (55.2)		16 (57.1)	20 (52.6)	0.805
SCC*mec* IV	20 (29.9)		6 (21.4)	14 (36.8)	0.278
SCC*mec* V	8 (11.9)		5 (17.9)	3 (7.9)	0.269
Untypeable	1 (1.5)		0 (0)	1 (2.6)	1.000
Type of MRSA					
HA-MRSA	57 (85.1)	< **0.0001**	25 (89.3)	32 (84.2)	0.722
SCC*mec* I	1 (1.8)		1 (4)	0 (0)	
SCC*mec* III	33 (57.9)		16 (64)	17 (53.1)	
SCC*mec* IV	16 (28.1)		4 (16)	12 (37.5)	
SCC*mec* V	6 (10.5)		4 (16)	2 (6.3)	
Untypeable	1 (1.8)		0 (0)	1 (3.1)	
CA-MRSA	9 (13.4)		3 (10.7)	6 (15.8)	
SCC*mec* III	3 (33.3)		0 (0)	3 (50)	
SCC*mec* IV	4 (44.4)		2 (66.7)	2 (33.3)	
SCC*mec* V	2 (22.2)		1 (33.3)	1 (16.7)	
Not known	1 (1.5)				
SCC*mec* III	1 (100)				
PVL gene	0 (0)		0 (0)	0 (0)	
Vancomycin MIC					
< 1.5 μg/mL	28 (41.8)	0.119	8 (28.6)	20 (52.6)	0.077
≥1.5 μg/mL	38 (56.7)		20 (71.4)	18 (47.4)	
Not known	1 (1.5)				
Outcome variables					
Persistent bacteremia	25 (37.3)		11 (39.3)	14 (36.8)	1.000
Recurrent bacteremia	10 (14.9)		6 (21.4)	4 (10.5)	0.302
Persistent and recurrent bacteremia	1 (1.5)		0 (0)	1 (2.6)	1.000
Survived	41 (61.2)		10 (35.7)	31 (81.6)	**0.0003**
Died	25 (37.3)		18 (64.3)	7 (18.4)	
Not known	1 (1.5)				

[a] Continuous variables are expressed as mean (± SD) and categorical variables are expressed as n (%). MRSA, methicillin-resistant *Staphylococcus aureus*, HA, healthcare-associated, CA, community-associated, HIV, human immunodeficiency virus, SCC*mec*, Staphylococcal cassette chromosome *mec*.

[†] Bold text indicates *P* value < 0.05.