



MRSA Infection in General Surgical Wards in a Malaysian Tertiary Hospital: A Retrospective Study

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Abstract

Background: Methicillin-Resistant *Staphylococcus aureus* (MRSA) has been contributing to nosocomial infections ever since 1961. In Malaysia, there was an increase in the MRSA rate from 18% in 2016 to 19.8% in 2017.

Materials and Methods: In our study, we determined the prevalence, the risk factor of developing MRSA infection and investigate the prognosis in surgical wards, for all adult patients (>18 years old) with MRSA bacteremia who was admitted to the Hospital Tuanku Jaafar (HTJ), from January 2018 to December 2018, we focused on surgical departments only as previous studies done for all hospital departments medical and surgical.

Results: In our study, the prevalence of MRSA is 8.53% in surgical wards, from a total of 598 patients were isolated with *staphylococcus aureus* 51 patients' specimens were detected with MRSA infection. Risk factors include older patients aged more than 60 years, prolonged duration of hospitalization, history of antibiotic use in the past and comorbidities such as chronic kidney disease, hypertension, and diabetes mellitus represent 5.9%, 47.1% and 35.3% respectively, with mortality rate 11.76%.

Conclusion: Our explanations for low percentage in surgical departments comparison to other specialties, that is most probably due to applications of the infection control measures including hand hygiene, personal protection equipment, isolation of antibiotic-resistant cases, also, applications of guideline for prevention of surgical site infection issued by Ministry of Health, Malaysia, which includes shortening the hospital staying duration, chlorhexidine bath the night before surgery, Enhanced Recovery after Surgery (ERAS) protocols for colonic cases.

Keywords: Methicillin-Resistant *Staphylococcus aureus*; Risk factors; Mortality; Prevalence

Materials and Methods

Objective

A- To determine the prevalence and epidemiological factors of MRSA infection in the HTJ common surgical ward.

B- To determine the risk factor of developing MRSA infection in the HTJ common surgical ward.

C- To investigate the prognosis of MRSA infection in HTJ common surgical ward.

Study type and design

A retrospective study, in this study, will collect data of all adult patients (>18 years old) with MRSA bacteremia from January 2018 to December 2018 from HTJ database. Patients will be sourced from HTJ common surgical ward 3A, 3B and 8B.

Study population

All adult patients (>18 years old) with MRSA bacteremia who was admitted to HTJ from January 2018 to December 2018.

Inclusion criteria

Patient with MRSA infection in HTJ common surgical ward from 1st Jan 2018 to 31st December 2018 (1 year).

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Table 1: MRSA antimicrobial sensitivity and resistance pattern.

Antibiotics	Antibiotics - sensitivity		Antibiotics - intermediate		Antibiotics - resistance		P-value
	CA-MRSA	HA-MRSA	CA-MRSA	HA-MRSA	CA-MRSA	HA-MRSA	
PEN	3	21	0	0	4	23	0.811
SXT	7	44	0	0	0	0	
GEN	6	41	0	0	1	3	0.457
ERY	5	29	0	0	2	15	0.774
CLI	4	30	0	1	3	13	
CIP	4	25	0	0	3	19	0.987
RIF	7	44	0	0	0	0	
FUS	7	41	0	0	0	3	0.476
LNZ	7	44	0	0	0	0	
VAN	7	44	0	0	0	0	
OXA	0	0	0	0	7	44	

*CA –Community-acquired, HA – Hospital-Acquired, PEN – Penicillin, SXT - sulfamethoxazole/ trimethoprim, GEN – gentamycin, ERY – Erythromycin, CLI – Clindamycin, CIP – ciprofloxacin, RIF – rifampicin, FUS – Fusidin, LNZ – linezolid, VAN – Vancomycin, OXA – Oxacillin.

Exclusion criteria

Referral of MRSA from other hospitals and wards, patients below 18 years old and any pregnant patients.

Withdrawal criteria

Not applicable

Sample size

All the patients that fit the inclusion criteria will be included in this study.

Data collection

Demographics and clinical data of patients including age, gender, ward, comorbidities, the severity of the disease, sources of bacteremia (primary or secondary) and clinical outcome (persistent or recurrent bacteremia and mortality status) will be collected from the patient's hospital medical record. Data on the detection of Methicillin Resistance using the disk diffusion method will be collected as well as phenotyping of MRSA strains from the Lab Information System (LIS).

Statistical analysis plan

All statistical analyses will be done using Statistical Package for Social Sciences (SPSS) Version 24. All categorical variables will be represented using frequency (n) and percentage (%), and comparison will be done using the Chi-square test and Fisher's exact test, where applicable. All continuous variables will be represented using mean and Standard Deviation (SD), and comparison will be done using a t-test. All tests will be set at 95% Confidence Interval (CI), and any p-value (p<0.05) will be considered significant. Logistic regression will be used to calculate odds-ratio and CI.

Results

Prevalence and antimicrobial resistance pattern of MRSA

There are 598 patients were isolated with *Staphylococcus aureus* from a clinical specimen in general surgical wards of HTJ from 1st January 2018 to 31st December 2018. From a total of 598 isolates, a total of 51 patient's specimens were detected with MRSA infection during their hospital stay, making a prevalence of 8.53%. In terms of the MRSA resistance pattern, all the samples were sensitive to Vancomycin (VAN), Sulfamethoxazole/Trimethoprim (SXT), Linezolid (LNZ) and Rifampicin (RIF) (Table 1).

Socio-demographic and risk factors associated with MRSA

The mean age of the study sample is 46.61 ± 16.76 years, with 56.9 percent (n=29) of them were below 40 years old. Most of the patients were male and Malay, comprising 70.6% (n=36) and 49% (n=25) respectively. The most common comorbidities in this sample study are hypertension (47.1%, n=24), and most of the study samples have no significant comorbidities (51%, n=26). 68.6% (n=35) of the patients had undergone at least a major surgery, with the most common procedure done is neurology-related procedure or surgery (31.4%, n=16). The most common sample used for the diagnosis of MRSA in these patients was tissue sample (31.4%, n=16) and most of the samples were diagnosed as hospital-acquired MRSA (86.3%, n=44) (Figure 1). Only three patients (5.9%) were identified to be given antibiotic prophylaxis before the procedure or surgery, with most of the patients had been consuming less than two antibiotics (76.5%, n=39). The mean duration of hospitalization for this study was 29.96 ± 40.8 days, with 56.9% (n=29) of them stays beyond two weeks (Table 2). In terms of risk factors, duration of hospitalization of more than two weeks is the only determinant found to have a statistically significant association for developing MRSA in these common surgical wards (OR=0.682 Chi-square = 10.695, 95% CI=0.513 to 0.907, P=0.001) (Table 3).

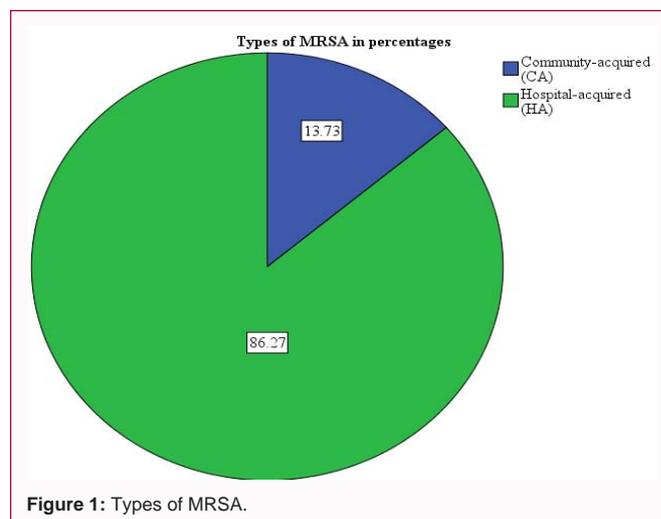


Figure 1: Types of MRSA.

Table 2: Socio-demographic background and relevant characteristics of MRSA patients.

Determinants		Frequency (n=51)	Percentage (%)
Age	below 40	22	43.1
	above 40	29	56.9
	Mean + SD	46.61 + 16.76	
Comorbidities	T2DM	18	35.3
	HTN	24	47.1
	Dyslipidemia	9	17.6
	Renal Disease	3	5.9
Number of relevant comorbidities	<2	42	82.4
	>2	9	17.6
Duration of hospitalization	< 2 weeks	22	43.1
	>2 weeks	29	56.9
	Mean + SD	29.96 + 40.8	
Gender	Male	36	70.6
	Female	15	29.4
Major surgery		35	68.6
Race	Malay	25	49
	Chinese	17	33.3
	Indian	9	17.6
Phenotype	Community-acquired	7	13.7
	Hospital-acquired	44	86.3
First sample for MRSA taken	Blood	8	15.7
	Fluid	1	2
	Pus	6	11.8
	Swab	8	15.7
	CSF	3	5.9
	Sputum	1	2
	Tracheal aspirate	7	13.7
	Tissue	16	31.4
	Other	1	2
Surgery/surgical related procedures done	Incision and drainage	7	13.7
	Saucerization	9	17.6
	Chest Tube	2	3.9
	Neurology-related	16	31.4
	GIT-related	5	9.8
Prophylactic antibiotic used		3	5.9
Antibiotics used in ward	<2	39	76.5
	>2	12	23.5

*HTN – hypertension, T2DM – Type II Diabetes Mellitus- GIT Gastro-intestinal

The prognosis/mortality and risk factors

There were a total of six patients (11.76%) who had passed away after diagnosis of MRSA infection was made, with the cause of death was due to severe sepsis and septic shock secondary to MRSA infection (5.9%, n=3), myocardial infarction (1.96%, n=1) and unknown (3.92%, n=2). In terms of risk factors for mortality, age more than 40 years old is the only determinant that shows statistically significant association in mortality among MRSA patients in the common surgical wards (Chi-square = 5.159, 95% CI=1.047 to 1.518, P = 0.023) (Table 4).

Discussion

According to the Infectious Diseases Research Centre, Institute for Medical Research, Kuala Lumpur, Malaysia the MRSA rate was 19.8% in 2017 for all medical and surgical specialties [5]. In our study, the MRSA was 8.53% in surgical wards only these were giving the impression that MRSA infections were a little higher in medical wards.

Our explanations for low percentage in surgical departments comparison to other specialties, that is most probably due to applications of the infection control measures in HTJ surgical

Table 3: Risk factors associated with MRSA infection in these common surgical wards.

Determinants		CAI (n=7)	HAI (n=44)	P-value
Age	below 40	2 (3.9)	20 (39.2)	0.402
	above 40	5 (9.8)	24 (47.1)	
Comorbidities	T2DM	2 (3.9)	16 (31.4)	0.689
	HTN	3 (5.9)	21 (41.2)	0.811
	Dyslipidemia	1 (2.0)	8 (15.7)	0.802
	Renal Disease	1 (2.0)	2 (3.9)	0.364
Number of relevant comorbidities	<2	5 (9.8)	37 (72.5)	0.414
	>2	2 (3.9)	7 (13.7)	
Duration of hospitalization	< 2 weeks	7 (13.7)	15 (29.4)	0.001
	>2 weeks	0 (0)	29 (56.9)	
Gender	Male	3 (5.9)	33 (64.7)	0.083
	Female	4 (7.8)	11 (21.6)	
Major Surgery		5 (9.8)	30 (58.8)	0.863
Race	Malay	2 (3.9)	23 (45.1)	0.244
	Non-Malay	5 (9.8)	21 (41.2)	
Surgical related procedure/ surgery	Incision and drainage	2 (3.9)	5 (9.8)	0.242
	Saucerization	3 (5.9)	6 (11.8)	0.06
	Chest Tube	0	2 (3.9)	1
	Neurology-related	0	16 (31.4)	0.054
	GIT-related	0	5 (9.8)	1
Prophylactic antibiotic used		0	3 (5.9)	1
Number of antibiotics used in ward	<2	6 (11.8)	33 (64.7)	0.535
	>2	1 (2.0)	11 (21.6)	

*HTN – hypertension, T2DM – Type II Diabetes Mellitus

Table 4: Risk factors associated with mortality among MRSA patients in these surgical wards.

	P-value	Chi-square Value
Age > 40 years old	0.023	5.159
T2DM	0.915	0.011
HTN	0.058	3.592
Dyslipidemia	0.06	4.898
Renal disease	1	0.425
Duration of hospitalization	0.215	1.535
Gender	0.162	2.833
Major surgery	0.363	1.096
Number of comorbidities	1	0.004
Incision and drainage	0.578	1.082
Saucerization	1	0.004
Chest Tube	1	0.278
Neurology-related	0.363	1.096
GIT-related	1	0.739
Types of MRSA	1	0.05
Prophylactic antibiotics used	0.232	1.428
Number of antibiotics used	0.315	2.092

*HTN – hypertension, T2DM – Type II Diabetes Mellitus

departments include hand hygiene, personal protection equipment, regularly cleaning of patient wards, isolation of antibiotic-resistant cases, and standard wound care. Also, applications of

prevention of surgical site infection by application of infection control guideline, issued by Ministry of Health, Malaysia in 2010 [6]. Which includes shortening the patient hospitalization duration admit a day before elective surgery, chlorhexidine bath the night before surgery, Enhanced Recovery after Surgery (ERAS) protocols for colonic cases.

In general, *S. aureus* Bacteremia (SAB) often causes other infections such as infective endocarditis, septic arthritis, and osteomyelitis [7]. Invasive infection can be developing within 2 years in 21% of persistent and 13% of intermittent carriers [8]. A study conducted within patients who were carriers for MRSA infection before found that these patients have a 27% risk of developing subsequent MRSA infection in the second year of carriage and 16% risk thereafter. Complications include MRSA-associated pneumonia and bacteremia and substantial MRSA-associated mortality [9]. In our study the mortality was 11.76% related to associated comorbidities not due to the previous admission.

In a study done in the United States, they noticed that 76.3% of patients with surgical site infection with MRSA were readmitted to the hospital within 90 days after the initial surgery, associated with a 22% one-year mortality rate in our study we do not have readmitted cases [10].

Risk factors for MRSA colonization

MRSA infection was commonly found in older patients aged more than 60 years old, female patients, patients with pneumonia, high in CCI index (Charlson Comorbidity Index) Pitt's bacteremia sore predictor of early mortality risk and high APACHE score (Acute

Physiology and Chronic Health Evaluation II) were at higher risk of mortality from MRSA infection [11]. The mean age of our study sample is 46.61, with 56.9% (n=29) of them were below 40 years old and 43.1% above 40 years old age and most of them were males comprising 70.6% (n=36).

Prolonged duration of hospitalization, as the increase in one day of hospitalization, will increase the risk for MRSA infection by 1.034 times [4]. In a nationwide study of hospitals in Japan, surgical patients with MRSA infection had a greater impact than medical patients with MRSA infection, resulting in approximately doubled the length of stay and hospital costs in our study we found that the mean duration hospital stay in MRSA patients was 29.96 days, with 56.9% (n=29) of them stays more than two weeks, and all had hospital-acquired MRSA infections, although who were stay less than 2 weeks in the hospital 13.7% had Community-acquired and 29.4% had hospital-acquired, total 43.1% (n=22), there is a good indication that prolonged hospitalization increasing the hospital-acquired MRSA infections [12].

History of antibiotic use in the past increases MRSA, but uses of antibiotics prophylactics decreases MRSA, in our study three patients only (5.9%) were identified to be given antibiotic prophylaxis before the procedure, other patients had been consuming less than two antibiotics were 39 patients (76.5%) and who used more than two days were 12 patients (23.5%), these indicate that antibiotics prophylaxis decrease the rate of MRSA infections.

National antibiotic guidelines Malaysia in 2014 recommended the use of Vancomycin as the antibiotic of choice in the MRSA infection [13] but Raja et al. [14] reported that Community-acquired vancomycin-resistant Enterococci cases were reported in Malaysia but in our study no resistance cases to vancomycin.

As regards antibiotics response, in general, there are increasing in the number of *Staphylococcus aureus* isolates which are resistant to-lactam antibiotics, in some countries, more than half of isolates from intensive care units are MRSA strains. Of great concern is that infections caused by MRSA strains are no longer limited to hospitalized patients [15]. In our study there are antibiotics resistances to Penicillin, Gentamycin, Erythromycin, Clindamycin, Ciprofloxacin, Fusidin & Oxacillin. In some cases, but all the samples were sensitive to Rifampicin, Linezolid, Vancomycin and Sulfamethoxazole/Trimethoprim.

Comorbidities, major surgery and invasive procedure which done bedside were found to be the risk factors for developing MRSA among patients in our study the neurosurgery operations had the highest risk by 31.4% and comorbidities such as chronic kidney disease, hypertension, and diabetes mellitus represent 5.9%, 47.1% and 35.3% respectively in MRSA infection cases [4].

With the potential of transferring resistance genes to other Gram-positive bacteria, our study intended to survey the prevalence of community-acquired MRSA which was 13.73% and hospital-acquired was 86.27% (Figure 1). Which is approximately equal to the results published by Naimi et al. [16] who is found that 12% of community-acquired *Staphylococcus aureus* infections were caused by MRSA strains, and in some regions, this percentage is dramatically higher.

Conclusion

The prevalence of MRSA was 8.53 % in our hospital, it was due

to applications of the infection control measures in HTJ surgical departments, and, applications guideline for prevention of surgical site infection. Risk factors for MRSA infections include old age, prolonged hospitalization, previous abuse of antibiotics, major surgery and comorbidities such as chronic kidney disease, hypertension, and diabetes mellitus represent. In terms of the MRSA resistance pattern, all the cases were sensitive to vancomycin, sulfamethoxazole-trimethoprim, Linezolid, and rifampicin.

Ethics of Study

This study will be conducted in compliance with the ethical principles outlined in the Declaration of Helsinki and The Malaysian Good Clinical Practice Guideline. Accepted by The International Medical University Joint-Committee of The Research and Ethics Committee (IMU-JC) 174 meeting in 17 January 2019, code (IA509) & NMRR ID: National Medical Research Register-Research submission notification to IRB/IEC IMU Ethics Committee (IMU) (NMRR-18-3712-45411 S1).

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