Methicillin-Resistant Staphylococcus aureus (MRSA) Patterns and Antibiotic Susceptibility in Surgical and Non-Surgical Patients in a Tertiary Hospital in Indonesia

Dewi Kartika Turbawaty, Verina Logito, Anna Tjandrawati
Department of Clinical Pathology Faculty of Medicine Universitas Padjadjaran
Dr. Hasan Sadikin General Hospital Bandung, Indonesia

Abstract

Methicillin-Resistant Staphylococcus aureus (MRSA) in the hospital is found mainly in surgical patients, which increases morbidity and mortality. Currently, vancomycin is the drug of choice for the treatment of MRSA infections. The increasing use of vancomycin and its inappropriate administration may increase the resistance of S. aureus to vancomycin. This study aimed to describe the distribution of MRSA and types of antibiotics that are still sensitive to MRSA in surgical and non-surgical patients. This cross-sectional, observational, retrospective descriptive study was conducted at the Microbiology Laboratory, Dr. Hasan Sadikin General Hospital, in 2019 using secondary data on the results of culture examination and antibiotic susceptibility of positive S. aureus culture isolates from all types of isolates from surgical and non-surgical patients. All specimens were cultured in appropriate media. Identification of S. aureus was performed by Gram staining to identify bacterial morphology, and automatic tools. Antibiotic susceptibility test was performed using an automatic machine. Seventy-five isolates (17%) were identified to be MRSA with 46 (53%) of them retrieved from surgical patients. Most of the MRSA isolates came from pus and were mostly due to skin infections. Antibiotic susceptibility results showed two Vancomycin-Resistant Staphylococcus aureus (VRSA) isolates from surgical patients. The positive culture of the MRSA and VRSA was dominated by surgical patients with pus coming from surgical wound infection, burn, and other skin infection as the most common sources. Thus, the proportion of MRSA isolates in the hospital in 2019 is 17% and two VRSA isolates are identified in the same year. The surgical ward was the primary origin of most MRSA isolates. Further studies are necessary to identify the MRSA incidence rate, evaluation and periodic monitoring of antibiotic use, and active surveillance in the surgical patient rooms.

Keywords: Antibiotic susceptibility, MRSA, surgical patients, VRSA

Pola Bakteri Methicillin-Resistant Staphylococcus aureus (MRSA) dan Kepekaan Antibiotik pada Pasien Bedah dan Non Bedah di Rumah Sakit Tersier Indonesia

Abstrak

Keberadaan Methicillin-Resistant Staphylococcus aureus (MRSA) di rumah sakit banyak ditemukan terutama pasien bedah yang meningkatkan morbiditas dan mortalitas. Saat ini vancomycin adalah drug of choice untuk terapi infeksi MRSA. Peningkatan penggunaan vancomycin dan pemberiannya yang tidak tepat memungkinkan terjadinya peningkatan resistensi S. aureus terhadap vancomycin. Oleh karena itu, penelitian ini bertujuan mengetahui gambaran sebaran bakteri MRSA dan jenis antibiotik yang masih sensitif terhadap MRSA pada pasien bedah dan non bedah. Penelitian potong lintang, observasional, deskriptif retrospektif ini dilakukan di Laboratorium Mikrobiologi Rumah Sakit Dr. Hasan Sadikin (RSHS) pada tahun 2019 dengan data sekunder hasil pemeriksaan bakteri dan resistensi antibiotik isolat kultur positif S. aureus dari semua jenis isolat dari pasien bedah dan non bedah. Semua spesimen akan dikultur lalu identifikasi S. aureus dengan melakukan pewarnaan Gram, melihat morfologi bakteri, dan alat otomatis. Uji kepekaan antibiotik menggunakan mesin otomatis. Tujuh puluh lima (17%) isolat merupakan MRSA dan 46 (53%) di antaranya berasal dari pasien bedah. Hasil kepekaan antibiotik menunjukkan 2 isolat Vancomycin-Resistant Staphylococcus aureus (VRSA) yang berasal dari pasien bedah. Hasil kultur positif MRSA dan VRSA didominasi oleh pasien bedah dengan sumber tersering isolat pus yang berasal dari luka surgical site infection, luka bakar, dan infeksi kulit lainnya. Pada tahun 2019 jumlah isolat MRSA 17%, dua di antaranya merupakan isolat VRSA. Bangsal bedah merupakan ruangan asal isolat MRSA terbanyak. Disarankan penelitian lebih lanjut mengenai angka kejadian MRSA, evaluasi dan pemantauan penggunaan antibiotika secara berkala, identifikasi dan surveillance aktif di ruangan pasien bedah.

Kata kunci: Kepekaan antibiotik, MRSA, pasien bedah, VRSA

Corresponding Author: Verina Logito, Department of Clinical Pathology Faculty of Medicine Universitas Padjadjaran/Dr. Hasan Sadikin General Hospital Bandung, Jalan Pasteur No. 38 Bandung, West Java, Indonesia, Email: verinalogito@gmail.com
Introduction

*Methicillin-resistant Staphylococcus aureus* (MRSA) is a strain of *Staphylococcus aureus* (*S. aureus*) that is resistant to *isoazoyl penicillins* such as methicillin, oxacillin, cefoxitin, and *fluoxacillin* which are still the world’s leading nosocomial pathogenic bacteria. *Methicillin-resistant Staphylococcus aureus* is also cross-resistant to all beta-lactam antibiotics.1,2

Severe infections due to MRSA have become a new challenge for health practitioners related to the increased risk of morbidity and mortality, accompanied by a tendency to increase the frequency of MRSA in various countries. In The United States found more than 50% of *S. aureus* specimens in intensive care were MRSA.3,4 To date, MRSA data in Indonesia is very limited. The prevalence of MRSA in Dr. Soetomo Hospital Surabaya in 2016 was 8.2% of 643 patients for 3 months.5 In 2010, a research was conducted at Dr.Wahidin Sudirohusodo Makassar who showed that the incidence of MRSA in surgical patients was 51.9% (post-surgery 44.4% and diabetic foot care 7.5%) from the total MRSA specimens.6 The number of MRSA in Dr. Hasan Sadikin General Hospital Bandung (RSHS) in 2018 was 22(11.16%) positive MRSA specimens from 197 positive *S. aureus* specimens. From the results of several MRSA studies, it shows an increase in the number of MRSA from year to year. Although the research results showed a low prevalence of MRSA in Indonesia when compared to other countries, it is necessary to have a countermeasures strategy to prevent further infection.7

*Methicillin-resistant Staphylococcus aureus* typically is classified as hospital acquired; health care acquired. Hospital-acquired MRSA usually is the result of a nosocomial infection, often acquired following a surgical or invasive medical procedure during a hospital stay. The main transmission of MRSA is through patient-to-patient contact through contamination through hands of unwashed medical staff and nurses, airborne transmission from patients with MRSA pneumonia or those using air conditioners (ventilators). MRSA infection usually worsens the patient’s condition. The higher the number of patients infected with MRSA in the hospital, the higher the danger of infection/transmission due to nosocomial MRSA infection. MRSA infection can cause lethal bacteremia (fatal), endocarditis and pneumonia, especially in critically ill patient.3,4

Currently, vancomycin is the drug of choice for the treatment of MRSA infections. The increasing use of vancomycin and its inappropriate administration for MRSA therapy may increase the resistance of *S. aureus* to vancomycin. Vancomycin-Resistant *Staphylococcus aureus* (VRSA) refers to bacteria that have resistance to vancomycin. Based on several studies, the presence of MRSA and VRSA in the hospital environment has been widely found, especially in surgical patients. The Centers for Disease Control and Prevention (CDC) suggests that the risk factors for MRSA and VRSA infections are individuals who have been hospitalized or undergoing surgery in the past year, have permanent medical aids in their bodies, reside in long-term care facilities.8-10

Based on the description above, searching for various literature, and the high incidence of MRSA in hospitals, especially surgical patients, the researchers are interested in knowing the description of the distribution of MRSA bacteria which can be used as a basis for evaluating and monitoring the incidence of MRSA and the types of antibiotics that are still sensitive to MRSA in surgical and non-surgical patients in RSHS. This study aims to determine the distribution of MRSA bacteria which can be used as a basis for evaluating and monitoring the incidence of MRSA and the types of antibiotics that are still sensitive to MRSA in surgical and non-surgical patients in RSHS.

Methods

This retrospective observational, descriptive research was conducted in the Microbiology Laboratory of the RSHS Clinical Pathology Department in 2019. The data were taken in a cross-sectional manner. The research subjects were secondary data on the results of culture and antibiotic resistance examinations with the result of *S. aureus* positive culture specimens from all types of specimens from surgical and non-surgical patients in RSHS who were sent to the Microbiology Laboratory of the RSHS Clinical Pathology Department in the period 2019. MRSA specimens including age, sex, specimen type, and origin of specimen submission, were processed with *Microsoft Excel* software and presented descriptively.

Examination of culture and antibiotic resistance in the Microbiology Laboratory of the RSHS Clinical Pathology Department for MRSA bacteria are as follows: All types of specimens
will be cultured in the appropriate media (blood agar) and then identified when there is growth after 24 hours. Identification of *S. aureus* was done by performing Gram staining, looking at bacterial morphology, and identification with automatic tools. Bacterial susceptibility test method using an automatic machine (Vitek-2 compact), will get the results of identification and susceptibility of antibiotics that have been validated in accordance with international standards (CLSI = Clinical laboratory Standard International). There are three stages of inspection on this tool, namely preparation and standardization of inoculum turbidity, entering data with a barcode system and inserting a card into the instrument. Furthermore, the process of inoculation, incubation, reading, validation and result interpretation will be carried out automatically by the tool.

The inclusion criteria for the subjects of this study are positive culture specimens from all types of specimens sent to the Microbiology Laboratory of the RSHS Clinical Pathology Department in the 2019 period with complete data including age, sex, type of specimen, the origin of specimen delivery, and data on antibiotic susceptibility. The exclusion criteria for the subjects of this study were the results of MRSA-positive isolates from outside the RSHS. The percentage of MRSA results is expressed by the number of MRSA samples per entire sample with the result of *S. aureus* positive culture specimen for one year. This study was approved by the Health Research Ethics Committee of Dr. Hasan Sadikin General Hospital Bandung, Indonesia number: LB.02.01/X.6.5/70/2020.

**Result**

In 2019, 467 *S. aureus* specimens were obtained in the Microbiology Laboratory of the RSHS Clinical Pathology Department. The results of the research can be seen in Figure 1. below. During 2019, a total of 18,914 isolates were obtained from 17,318 patients. Total positive cultures were 9,969 (52.31%) isolates from 9,059 patients. Of the total positive cultures, 467 (4.68%) isolates were obtained with the results of *S. aureus*. A total of 75 *S. aureus* specimens were MRSA (17%). A total of 75 MRSA specimens obtained from the results of culture and resistance examinations at the Microbiology Laboratory of the RSHS Clinical Pathology Department in 2019 came from 72 patients, with details of 31 female patients and 41 male patients. In this study, there were 3 patients with MRSA positive specimens from specimens were obtained from different places. These three patients were one baby boy and two adult patients. Based on age, the incidence of MRSA infection was more common in adulthood, with 67 people (93%) compared to 5 children (7%). The MRSA Sample Characteristics Data can be seen in Table 1.

Specimens with MRSA results were sent from surgical and non-surgical patients from inpatient, outpatient, and emergency services at RSHS who were sent to the Microbiology Laboratory of the RSHS Clinical Pathology Department.
### Table 1 MRSA Sample Characteristics Data

| Characteristics | Total | (%) |
|-----------------|-------|-----|
| Age (years)     |       |     |
| Adult           | 67    | 93  |
| Child           | 5     | 7   |
| Gender          |       |     |
| Men             | 41    | 57  |
| Women           | 31    | 43  |

75 MRSA specimens, 46 specimens came from surgical patients, and 29 specimens came from non-surgical patients. Forty-six specimens from surgical patients were 24 specimens from the Surgical Inpatient Room, 11 specimens from surgical emergencies, and 11 specimens from the Surgical Polyclinic, Orthopedics, Urology, ENT. Twenty-nine specimens came from non-surgical patients, 24 specimens came from non-surgical inpatients, 2 specimens from non-surgical emergencies, and 3 specimens from non-surgical outpatients. The Emergency Room is the original room of the specimens with the most number of MRSA specimens of 13 specimens (17%). The distribution of MRSA based on the patient’s location can be seen in Figure 2.

The distribution of specimens from the MRSA specimen consisting of pus (40 specimens), blood (9 specimens), sputum (16 specimens), urine (7 specimens), CSF (2 specimens), and body fluids (1 specimen) can be seen in Figure 3.

After knowing the distribution of MRSA specimens in RSHS, an antibiotic susceptibility test was performed on these specimens. The antibiotics of choice for MRSA are vancomycin, linezolid, and tigecycline. Antibiotic susceptibility results showed that 73 (97%) isolates were sensitive to vancomycin. The remaining 2 were Vancomycin-resistant isolates derived from surgical inpatients. All isolates were sensitive to linezolid and tigecycline can be seen in Table 2.

### Table 2 Isolates Distribution of Antibiotic Susceptibility in RSHS

|          | Surgical Patient (n=46) | Non-Surgical Patient (n=29) |
|----------|-------------------------|-----------------------------|
|          | nS | %S | nS | %S |
| Linezolid| 46 | 100| 29 | 100|
| Tigecycline| 46 | 100| 29 | 100|
| Vancomycin| 44 | 97 | 29 | 100|

nS = number of isolate; %S = susceptibility

### Discussion

*Methicillin-Resistant Staphylococcus aureus* is an important nosocomial pathogen in the world and the increased frequency of MRSA is a cause of infection in the community and will increase morbidity and mortality. The global antimicrobial resistance surveillance system (GLASS) published by WHO in 2018 conducted a study in Thailand that obtained 1530 positive cultures from bacteremia patients, among them 149 (9.7%) positive specimens of *S. aureus*. From *S. aureus* positive specimens, obtained 28 (19%) specimens with MRSA.

The total number of positive culture specimens during the period 2019 was 9969 (52.31%) specimens from a total of 18,914 specimens. The objects in this study were 467 (4.68%) samples with Gram-positive bacterial culture results caused by *S. aureus*. A total of 75 (17.56%) of the research objects obtained positive Gram-positive cultures caused by MRSA. When compared with data from GLASS (WHO, 2018) the incidence rate of MRSA in RSHS is lower. The number of MRSA in RSHS in 2018...
was 22 (11.16%) positive MRSA specimens from 197 positive *S. aureus* specimens. The results of several MRSA studies, it shows an increase in the number of MRSA from year to year; therefore it is necessary to have a countermeasures strategy so that no further infections occur.10

Seventy five specimens with positive MRSA culture results were obtained from 72 patients, which was caused by 3 patients with MRSA positive specimens from specimens taken from different sites. These three patients fall into the true infection category. One of the criteria for true infection is the discovery of the same organism in cultures from different specimens.13

Three patients who were eligible for true infection were a baby boy and two adult patients. The first patient was a one-month-old baby boy with a diagnosis of hydrocephalus with secondary infection in postoperative wounds, hospitalized in the surgical inpatient room, MRSA positive results were obtained in pus culture from the head, cerebrospinal fluid culture, and body fluid culture from VP shunt, and CSF culture. This is in accordance with one of the risk factors for MRSA, namely the use of invasive medical devices in these patients. The second patient, a 28-year-old woman with a diagnosis of combustio and diabetes mellitus, was treated in a surgical inpatient room, positive MRSA results were obtained in the pus and blood cultures. This is in accordance with one of the risk factors for MRSA, namely the length of stay in the hospital and the risk factors for previous chronic disease. The third patient, a 28-year-old male with a diagnosis of pemphigus vulgaris and abscess at the frontal region, was a patient from outpatient surgery, positive MRSA results were obtained on a culture of pus on the forehead and scalp. This third patient has a history of being treated for approximately 1 month at the nearest health center from where he lives. The three patients who were included in the criteria for true infection were surgical patients and the majority of MRSA-positive specimens were obtained from pus culture.

In this study, it was found that the most MRSA specimens came from pus, namely 40 (53%) specimens. *Methicillin-Resistant Staphylococcus aureus* is a Gram-positive bacteria that produces the enzyme coagulase, facultatively anaerobic, grow with an optimum at 37 °C. Most of the diseases caused by these bacteria produce pus, therefore it is called pyogenic bacteria.14,15 Similar results were also found in a study conducted by Del Mar et al., where pus as the largest specimen was 32% of the specimens.16 Forty of the pus specimens in this study came from patients with skin diseases, ulcers, postoperative wounds, malignancies, most of which were skin and soft tissue infections. In addition, there were quite a lot of cases of skin and soft tissue infections that also come from a considerable number of burns patients. This was also confirmed by Bouvet study that most specimens derived from skin and soft tissue infections (65%).17

In this study, there were 2 patients with positive MRSA cultures on CSF. Leazer’s study stated that the incidence of positive cultures in CSF is very small.18 The first patient was a one-month-old baby boy diagnosed with hydrocephalus with secondary infection in the postoperative wound with VP shunt installation. MRSA positive culture results were obtained in the pus culture in the surgical wound and CSF culture. *Methicillin-resistant Staphylococcus aureus* meningitis rarely occurs in neonates or children. In one study, the incidence of *S. aureus* meningitis in children was 6%, whereas MRSA meningitis was 18%.19 Central nervous system infection caused by MRSA occurred as a complication of neurosurgical procedures related to the focus of adjacent infection, or hematogenous infection. Hematogenous infection may result from a focal abscess in the postoperative wound or infected ventriculoperitoneal shunt.18 The second patient was a one-day-old baby girl with a diagnosis of seizure et causa meningitis from the pediatric emergency room. This neonate was born prematurely by a traditional midwife with very low weight and did not cry immediately. A positive MRSA culture was obtained from CSF culture in the second week of the neonatal treatment. Meningitis due to *S. aureus* and MRSA is commonly seen in very low weight and high-risk premature neonates requiring prolonged hospitalization, central venous catheter, external devices, and ventilator support.19

The location of the most specimens in this study was from surgical and non-surgical inpatients with 24 specimens each. The high incidence of MRSA in surgical and non-surgical inpatient wards is suspected because most patients were treated for a long period (average 20 days), which could increase the risk of MRSA infection. Based on Sennang et al research at RSWS Makassar, the length of stay for patients more than 21.33 days will increase MRSA infection.20 *Methicillin-resistant Staphylococcus aureus* is a pathogen that frequently causes infections in hospitals, resulting in longer hospitalization and higher costs for treatment and infection control.
requirements.\textsuperscript{20} The second-largest number of specimens originated from outpatient care as many as 14 specimens with the predominance of outpatient surgery. From these data, it is necessary to suggest improving the hygiene of health workers in each of these rooms.

Of the total 75 MRSA isolates, 59\% were from surgical patients. The high incidence of MRSA in surgical patients is due to many factors. \textit{Methicillin-resistant} invasive \textit{Staphylococcus aureus} is a cause of infection in the bloodstream, \textit{surgical site infection} (SSI), and pneumonia which may be life-threatening. \textit{The Center for Disease Control and Prevention} (CDC) limits SSI to an infection that occurs within 30 days of surgery and after one (1) year of implant surgery. \textit{Methicillin-resistant} \textit{Staphylococcus aureus} in infected wounds causes the mortality rate and longer care and hospitalization to increase.\textsuperscript{19}

The \textit{global antimicrobial resistance surveillance system} published by WHO in 2018 conducted a study in Thailand with two populations, namely \textit{community-acquired bacterial infections} (CABI) and \textit{hospital-acquired bacterial infections} (HABI). In the HABI population group, it was found that 57\% were sensitive to \textit{Oxacillin} and 100\% sensitive to \textit{Vancomycin}. Bacteremia due to MRSA was found 0\% in the \textit{community-acquired S. aureus bacteremia}, while 43\% of \textit{hospital-acquired S. aureus bacteremia}.\textsuperscript{10}

Data for VRSA in Indonesia is still very limited. Research at Wahidin Sudirohusodo Hospital, Makasar was conducted from January 2015 to December 2016, and obtained 387 \textit{S. aureus} specimens, 45 (11\%) were VRSA. The VRSA specimen was predominantly male patients (57.8\%) with an average age of 41-60 years (35.6\%). The treatment room with the most VRSA specimens came from the surgical ward (20\%). The most common specimens found were blood (28.9\%), pus (26.7\%), and sputum (20\%).\textsuperscript{20} Research at RSHS in 2018 was obtained from all \textit{S. aureus} specimens, there were no specimens with VRSA.

In this study, all specimens were sensitive to \textit{Linezolid} and \textit{Tigecycline} and two (3\%) inpatient specimens were resistant to \textit{Vancomycin} (VRSA). The first patient was a 29-year-old male with a diagnosis of burns and a sample of a pus culture. The second patient was a 1-day-old baby girl with a diagnosis of respiratory distress syndrome. The sample was a blood culture. When compared with data from GLASS (WHO, 2018), the VRSA rate in RSHS is higher (3\%).\textsuperscript{10} When compared with the VRSA figures in the hospital, Wahidin Sudirohusodo Makasar, the VRSA rate in RSHS is lower, but when compared to the number of VRSA in RSHS in 2018 it shows an increase from 0\% to 3\%.\textsuperscript{6}

The increasing number of MRSA and VRSA rates in RSHS can be influenced by several risk factors, including length of stay in the hospital, history of surgery, use of invasive medical devices, patients with a history of chronic diseases (such as diabetes, kidney disease), a history of MRSA or previous \textit{Vancomycin-resistant Enterococci} (VRE) infection, and previous exposure to \textit{Vancomycin} (especially in repeated or prolonged cases). In this study, VRSA results were obtained from pus and blood cultures, similar to a study by Saadat et al which found that VRSA was most commonly found in blood and pus specimens.\textsuperscript{11} \textit{Vancomycin} is a very important antibiotic in patients with MRSA because it is the first line of therapy for MRSA. Given the limited types of antibiotics that are sensitive to MRSA, \textit{vancomycin} should be placed as a last-line antibiotic or only used for suspected MRSA germs. Good hand hygiene behavior in the treatment room provides great leverage for the implementation of \textit{clean care} standards as a whole which in turn has a positive impact on the overall control of MRSA and VRSA infections control.\textsuperscript{9}

The limitation of this study is that there is no further explanation regarding the clear source of infection whether MRSA in the study subjects came from HABI or CABI and history of previous antibiotic use.

In conclusion, the results of this study indicated that the number of MRSA specimens was 17\%. The surgical ward is the room where the most MRSA specimens originated. Evaluation and monitoring of antibiotic use showed that all specimens were sensitive to \textit{Linezolid} and \textit{Tigecycline} and 2 (3\%) specimens were resistant to \textit{Vancomycin} administration.

Based on the result of this study, further research is necessary on the incidence of MRSA, evaluation, and monitoring of antibiotic use regularly to control and prevent an increase in the incidence of MRSA, for example with the implementation of active identification and \textit{surveillance} in surgical patient rooms.

References

1. Gould IM, David MZ, Esposito S, Garau J, Lina G, Mazzei T, Peters G. New insights into \textit{meticillin-resistant Staphylococcus
2. Harbarth S, Hawkey PM, Tenover F, Stefani S, Pantosti A, Struelens MJ. Update on screening and clinical diagnosis of meticillin-resistant Staphylococcus aureus (MRSA). Int J Antimicrob Agents. 2011;37(2):110–7.

3. Loewen K, Schreiber Y, Kirlew M, Bocking N, Kelly L. Community-associated methicillin-resistant Staphylococcus aureus infection: Literature review and clinical update. Canadian Family Physician. 2017;63(7):512–20.

4. Kavanagh KT, Abusalem S, Calderon LE. The incidence of MRSA infections in the United States: is a more comprehensive tracking system needed?. Antimicrob Resist Infect Control. 2017;6:34.

5. Kuntaman, Hapsari R, Hadi P, Winarto W, Milheiriço C, Maquelin K, et al. Prevalence of methicillin resistant Staphylococcus aureus from nose and throat of patients on admission to medical wards of dr Soetomo Hospital, Surabaya, Indonesia. Southeast Asian J Trop Med Public Health. 2016; 47(1):1–5.

6. Ahmad F, Sennang N, Rusli B. Vancomycin Resistant Staphylococcus Aureus (VRSA) in Dr. Wahidin Sudirnohosodo Hospital Makassar. Indonesian Journal of Clinical Pathology and Medical Laboratory. 2019 13;25(2):194–8.

7. Santosaningsih D, Santoso S, Budayanti NS, Kuntaman K, Lestari ES, Farida H, et al. Epidemiology of Staphylococcus aureus harboring the mecA or Panton-Valentine leukocidin genes in hospitals in Java and Bali, Indonesia. J Trop Med Hyg. 2014;90(4):728–34.

8. Mahmudah R, Soleha TU, Ekowati CN. Identifikasi Methicillin-Resistant Staphylococcus Aureus (MRSA) Pada Tenaga Medis Dan Paramedis Di Ruang Intensivecare Unit (ICU) Dan Ruang Perawatan Bedah Rumah Sakit Umum Daerah Abdul Moeloek. Jurnal Majority. 2013;4(2):9–13.

9. Cong Y, Yang S, Rao X. Vancomycin resistant Staphylococcus aureus infections: A review of case updating and clinical features. J Adv Res. 2019;21:169–76.

10. Sirigatuphat R, Sripandikulchai K, Boonyasiri A, Rattanaumpawan P, Supapueng O, Kiratisin P, et al. Implementation of global antimicrobial resistance surveillance system (GLASS) in patients with bacteremia. PLoS One. 2018;13(1):e0190132.