CHARACTERISTICS OF ANTIBIOTIC RESISTANCE AND TREATMENT OUTCOMES OF *S. AUREUS* BACTERIA AT NATIONAL HOSPITAL FOR TROPICAL DISEASES IN PERIOD FROM 2022 TO 2024

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Overview: S. aureus bacteremia (SAB) progresses severely, can lead to septic shock and death. *S .aureus* is increasingly resistant to antibiotics. Updating antibiotic resistance characteristics and treatment outcomes of S. aureus bacteremia helps doctors provide appropriate treatment.

Objectives: study to describe the antibiotic resistance characteristics of S. aureus and evaluate the treatment outcomes of *S. aureus* bacteremia patients at the National Hospital for Tropical Diseases 2022 - 2024.

Subjects and methods: The study subjects included patients ≥ 18 years old, diagnosed with *S. aureus* bacteremia at the National Hospital for Tropical Diseases from April 2022 to March 2024, excluding cases with positive blood culture results for multiple etiologies. The study was a cross-sectional descriptive analysis. All samples were selected by a convenience method. Data were analyzed and processed using SPSS22.0 software with applied algorithms.

Results and conclusions: S. aureus had a high resistance rate to many antibiotics, MRSA accounted for 88%, multi-resistant bacteria accounted for 89.24%. However, *S. aureus* strains were still 100% sensitive to vancomycin, linezolid, tigecycline, nitrofurantoin. The average treatment time was 17.29 ± 10.4 days and all patients used antibiotics during the entire hospitalization. The rate of initial antibiotic prescription consistent with the antibiogram was 76.5%. Treatment results did not improve or worsened was 25.8%.

Keywords: *S. aureus*, bacteremia, antibiotic resistance.

INTRODUCTION

S. aureus bacteremia (SAB) has a severe progression, damaging many organs leading to dangerous complications or septic shock and death for patients. *S. aureus* strains are increasingly resistant to antibiotics. Updating the characteristics of antibiotic resistance as well as the treatment outcomes of SAB is very necessary to provide a scientific basis, helping doctors make appropriate treatment decisions. Therefore, we conducted a study to describe the antibiotic resistance characteristics of *S. aureus* and evaluate the treatment outcomes of SAB patients at National Hospital for Tropical Diseases 2022 - 2024.

METHODS AND PARTICIPANTS

The study subjects: All patients ≥ 18 years old, diagnosed with *S. aureus* bacteremia at National Hospital for Tropical Diseases from April 2022 to March 2024, excluding cases with positive blood culture results for more than 1 pathogen which was *S. aureus*.

Study method: Cross-sectional analysis.

Sample size and sample selection: Total sample selection by convenience method. Collect information on antibiotic resistance characteristics of bacteria and treatment outcomes of patients according to pre-designed research medical records. Bacterial culture, antibiotic susceptibility testing and

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Date of submission: *August 14, 2024*

Date of reviewed completion: *August 23, 2024*

Accepted date for polication: *November 25, 2024*

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MIC determination are performed at the Department of Microbiology - Molecular Biology, National Hospital for Tropical Diseases in strict compliance with the hospital's ISO procedures. Colonies growing on the culture medium will be Gram stained and automatically identified on the MALDI-TOF MS system (Bruker Diagnostics, Bremen, Germany), and antibiotic susceptibility testing will be automatically performed on the Vitek 2 COMPACT system (Vitek 2, BioMérieux, Marcy L'Etoile, France) according to CLSI guidelines.

Study data were analyzed and processed using SPSS 22.0 software with applied algorithms.

RESULTS AND DISCUSSION

During April 2022 to March 2024, 93 eligible patients were recruited into the study. The mean age of the patients in the study was 54.38 ± 17.99 years (minimum 19 years, maximum 90 years). The male to female ratio was 2:1.

Table 1. Antibiotic resistance levels of *S. aureus* strains

Antibiotic name	N	Antibiotic resistance levels		
		S n (%)	I n (%)	R n (%)
Penicillin G	85	3 (3.5)	0	82 (96.5)
Oxaciclin	75	9 (12.0)	0	66 (88.0)
Erythromycin	87	14 (16.1)	1 (1.1)	72 (82.8)
Clindamycin	85	14 (16.5)	0	71 (83.5)
Ciprofloxacin	75	55 (73.3)	0	20 (26.7)
Levofloxacin	71	56 (78.9)	0	15 (21.1)
Moxifloxacin	65	45 (69.2)	1 (1.5)	19 (29.3)
Daptomycin	4	4 (100)	0	0
Gentamicin	56	40 (71.4)	0	16 (28.6)
Vancomycin	87	87 (100)	0	0
Trimethoprim/sulfamethoxazole	87	63 (72.4)	0	24 (27.6)
Cefepime	27	1 (3.7)	0	26 (96.3)
Ceftriaxone	27	3 (11.1)	0	24 (88.9)
Ceftazidim	3	3 (100)	0	0
Cefotaxime	24	1 (4.2)	0	23 (95.8)
Cefpodoxime	19	3 (15.8)	0	16 (84.2)
Cefoxitin	9	5 (55.6)	0	4 (44.4)
Cefdinir	18	1 (5.6)	0	17 (94.4)
Imipenem	25	1 (4)	0	24 (96)
Meropenem	27	1 (3.7)	0	26 (96.3)
Doxycycline	11	8 (72.7)	0	3 (27.3)
Minocycline	4	3 (75)	0	1 (25)
Tigecycline	60	60 (100)	0	0

Antibiotic name	N	Antibiotic resistance levels		
		S n (%)	I n (%)	R n (%)
Tetracycline	73	22 (30.1)	0	51 (69.9)
Linezolid	85	85 (100)	0	0
Quinapristin/dafopristin	48	46 (95.8)	0	2 (4.2)
Rifampin	64	61 (95.3)	1 (1.6)	2 (3.1)
Piperacillin/tazobactam	4	2 (50)	0	2 (5
Nitrofurantoin	41	41 (100)	0	0
Chloramphenicol	4	2 (50)	0	2 (5

Comments: The isolated *S. aureus* strains were resistant to penicillin up to 96.5%. The MRSA rate accounted for 88%. The third generation cefalosporins and carbapenems were highly resistant, all were resisted for > 90%. The quinolone group had a lower resistance rate, < 30% in all 3 antibiotics of this group. Vancomycin, linezolide, tygecycline and nitrofurantoin were all 100% sensitive. In addition, some antibiotics had quite low resistance rates such as rifampin 2%, quinapristin/dafopristin 5.3%. Reports on the MRSA rate in Vietnam show that this rate has increased significantly over time. A study 5 years ago at 108 Military Central Hospital (2016 - 2018) showed that MRSA accounted for 47.4%[1]. In recent years, reports have shown that this rate fluctuates around 70% - 80%[2,3]. In our study, assessing the antibiotic resistance status of *S. aureus* in the period 2022 - 2024, this rate is up to 88%. This was predicted problem but still very worrying.

Table 2. Drug resistance classify of S. aureus

Drug resistance classify	Number (N = 93)	Rate (%)
Monodrug-resistant	5	5.38
Multidrug-resistant (MDR)	83	89.24
Extensively drug-resistant (XDR)	5	5.38
Pandrug-resistant (PDR)	0	0
Total	**93**	**100**

Comments: Multidrug-resistant *S. aureus* strains accounted for the highest proportion with nearly 90%. According to the definition of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID), MRSA strains are all multidrug-resistant *S. aureus*[4]. In our study, the MRSA rate was 88%. Thus, there are still *S. aureus* strains that are not resistant to methicillin but are still resistant to at least 3 different groups of antibiotics.

Table 3. Minimum inhibitory concentrations (MIC) of some antibiotic groups

MIC was determined for 10 isolated *S. aureus* strains:

Antibiotic	Result (µg/mL)	Number of patients (N = 10)	Rate (%)
Vancomycin	≤ 0.5	5	50
	1	4	40
	2	1	10

Antibiotic	Result (µg/mL)	Number of patients (N = 10)	Rate (%)
Linezolide	1	2	20
	2	8	80
Rifampin	0.5	10	10
Tygecycline	0.12	9	90
	0.5	1	10

Comments: The number of S. aureus strains with vancomycin MIC = 2 µg/mL accounted for 10%, MIC ≤ 0.5 µg/mL accounted for 50%, MIC = 1 µg/mL accounted for 40%. Different from the study of author Nguyen Thi Thanh Hien[5] when examining the distribution of vancomycin MIC on MRSA strains (n = 49), it showed that the majority of cultures had MIC ≤ 0.5 µg/mL (61.2%), 38.8% of cultures had MIC = 1 µg/mL, and no case of vancomycin MIC = 2 µg/mL was recorded. A 2021 study by author Ha Nguyen Y Khue[6] also showed that MIC = 2 µg/mL accounted for a low percentage (1.4%), MIC = 1.5 µg/mL accounted for 0.5%, MIC = 1 µg/mL accounted for 92.5%, MIC ≤ 0.5 µg/mL accounted for 5.6%. The reason for this difference may be due to the limited number of *S. aureus* strains evaluated for MIC in our study. There are more and more documents in the world reporting the failure rate when treating MRSA with vancomycin even though the MIC is still within the accepted sensitivity range (≤ 2 µg/mL). The study by Walraven et al. showed the possibility of vancomycin failure in treating MRSA in different types of infections with a failure rate of 5% when MIC vancomycin = 1 µg/mL, 40% when MIC vancomycin = 1.5 µg/mL and nearly 50% when MIC vancomycin = 2 µg/Ml[7]. This result warns of the risk of failure in treating MRSA and also warns of the possibility of vancomycin-resistant *S. aureus* strains appearing when vancomycin is widely used in hospital treatment as it is today.

Table 4. Appropriateness of empirical antibiotics used compared with antibiogram results

Antibiotic	Number of patients initially prescribed with antibiotic susceptibility test results	Suitable for the culture strain (sensitive/resistant)	
		S (n,%)	R (n,%)
Cefepime	1	0	1 (100)
Ceftriaxone	4	0	4 (100)
Ciprofloxacin	3	3 (100)	0
Imipenem	1	0	1 (100)
Levofloxacin	8	4 (50)	4 (5
Linezolid	16	16 (100)	0
Meropenem	11	1 (9.1)	10 (90.9)
Vancomycin	41	41 (100)	0
Total number of antibiotics prescribed times	85	65 (76.5)	20 (23.5)

Comments: The rate of initially prescribed antibiotics consistent with the results of the antibiotic susceptibility test out of 85 prescribed antibiotics was 76.5%. This result is similar to the study by author Nguyen Thi Thanh Hien[5]. with the rate of agreement between empirical antibiotics and the results of the antibiotic susceptibility test being 75.8%. After the results of the antibiotic susceptibility test were available, our study found that 100% of patients were given at least one of the two antibiotics, vancomycin and/or linezolid, in which the number of patients given vancomycin was 61/93 cases and the number of patients given linezolid was 57/93 cases.

Table 5. Duration of antibiotic treatment

Number of days	Number (N = 93)	Rate (%)
< 7 days	9	9.68
7 - 13 days	33	35.48
14 - 20 days	23	24.73
≥ 21 days	28	30.11
Average treatment time	17.29 ± 10.4	

Comments: All patients in the study were used antibiotics during the whole hospitalization. Of which, the proportion of patients using antibiotics within 7 - 13 days accounted for the highest proportion (35.48%), followed by the number of patients using antibiotics for 3 weeks or more (30.11%). The prescription of antibiotic treatment duration depends mainly on the clinical response of the patient, so most guidelines do not provide a specific number of days to maintain antibiotics for the patient. In this study, we recorded the longest case of antibiotic use was the case with 49 days usage or linezolid.

Table 6. Patient discharge status

Discharge status	Remission/ Complete Recovery	Not improve/ Gets worse	Death in hospital	Total
Number	69	24	0	93
Rate (%)	74.2	25.8	0	100

Comments: 74.2% of patients had remission or complete recovery. The treatment failure rate was 25.8% and there were no deaths in the hospital. This result is similar to the study of author Nguyen Thi Thanh Hien[5] with 74.6% of patients successfully treated (cured; improved, reduced disease) and 25.4% of patients failed treatment (no change; severe illness requiring discharge; death). The study of Allan et al.[8] found that the overall mortality rate was 34% and was not significantly higher in patients with community-acquired *S. aureus* bacteremia compared to patients with hospital-acquired S. aureus bacteremia.

CONCLUSIONS

S. aureus has a high resistance rate to many antibiotics, MRSA accounts for 88%, multi-resistant *S. aureus* account for 89.24%. However, *S. aureus* strains are still completely sensitive to vancomycin, linezolid, tigecycline, nitrofurantoin. The average treatment time is 17.29 ± 10.4 days and all patients are given antibiotics during the entire hospitalization. The rate of initial antibiotic prescriptions consistent with the antibiotic susceptibility test is 76.5%. Treatment results did not improve or worsened was 25.8%.

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