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ANTIMICROBIAL RESISTANCE PROFILES OF *Staphylococcus epidermidis* SEPTICEMIA IN VIETNAMESE CANCER PATIENTS

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ABSTRACT

Staphylococcus epidermidis is an important cause of bloodstream infections and a cause of morbidity and mortality in cancer patients. The antimicrobial resistance profiles of S. epidermidis septicemia in Vietnamese cancer patients are limited. We surveyed all S. epidermidis blood culture isolates from Vietnamese cancer patients at the Tan Trieu National Cancer Hospital, from 2020 to 2024. A total of 11 S. epidermidis isolates were identified and antibiotic susceptibility testing was employed. Methicillin resistance was detected in 4/11 of all isolates; all were sensitive to vancomycin, nitrofurantoin, linezolid, quinupristin-dalfopristin; however, all were resistant to benzylpenicillin, oxacillin; 7/11 of isolates were resistant to clindamycin, erythromycin, and trimethoprim-sulfamethoxazole; All of the isolates (11/11) are multidrug resistance. Vancomycin, nitrofurantoin, linezolid, and quinupristin-dalfopristin are effective antimicrobial agents in treating S. epidermidis septicemia in Vietnamese cancer patients. The high level of methicillin and multidrug resistance limited the therapeutic options in Vietnamese cancer patients are causes of concern.

***Keywords**: S. epidermidis, vancomycin, methicillin, septicemia, Vietnamese, cancer*

1. INTRODUCTION

Bloodstream infection is life-threatening and is associated with high mortality. Coagulase-negative *Staphylococcus* are one of the most common from blood culture samples. *Staphylococcus epidermidis* septicemia is an underestimated cause of septic shock. Immunocompromised patients such as cancer patients in intensive care units with central lines are most at risk. *S. epidermidis* septicemia is associated with intensive care unit mortality (1). Cancer patients are at risk of bloodstream infections. *S. epidermidis* rarely causes disease in healthy persons and is a common colonizer of the human skin and mucous membranes. However, *S. epidermidis* has been recognized as an

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important etiology of bloodstream infections in immunocompromised patients such as cancer patients and patients with indwelling medical devices (2).

S. epidermidis is present on skin as commensal flora, therefore the presence of *S. epidermidis* in the blood is usually considered to be contamination, especially if a single culture is positive. *S. epidermidis* bacteremia is considered a pathogen only when isolated multiple times. *S. epidermidis* is a nosocomial pathogen that is spread in hospital environments. At a local hospital level, *S. epidermidis* occurrence, persistence, and long term spread (3).

S. epidermidis forms biofilm, which reduces the efficacy of antimicrobials. *S. epidermidis* is a nosocomial pathogen and has widespread resistance to various antimicrobial agents (4). While *S. aureus* is a known pathogen, *Staphylococcus epidermidis* is considered to be a common contaminant of blood culture. Many researchers have challenged this traditional viewpoint.

S. epidermidis septicemia is associated with cancer patients' mortality. However, the antibiotic-resistant profile of *S. epidermidis* in Vietnamese cancer patients remains scarce. This study was retrospectively conducted over 4 years at Tan Trieu National Cancer Hospital to investigate the antimicrobial susceptibility pattern of *S. epidermidis* causing bloodstream infections among Vietnamese cancer patients. This data will help to understand the current antimicrobial-resistant profile of *S. epidermidis* and provide a reference for antimicrobial-resistant control policy in Vietnam.

2. MATERIALS AND METHODS

Ethical considerations

Ethical approval for laboratory data was not required as the study was routine surveillance measures for infection control.

Isolation and identification of *S. epidermidis*

We surveyed positive blood cultures isolated from Vietnamese cancer patients treated between 2020 and 2024 at the Tan Trieu National Cancer Hospital. All blood culture samples of Vietnamese cancer patients suspected of having bloodstream infection were incubated in BACT/ALERT®3D system (bioMérieux, France). Bacteria were screened using the VITEK 2-Compact© system (bioMérieux, France) according to routine procedures. At least two separate blood cultures obtained from different sites are positive to be considered as true infection.

Antimicrobial susceptibility testing

Antimicrobial susceptibility testing of the isolated *S. epidermidis* were performed by VITEK 2-Compact© system (bioMérieux, France) according to routine procedures. Breakpoints for antibiotic resistance were according to CLSI 2020. Multidrug resistance was defined as resistance to ≥3 antibiotic classes.

Statistical analysis

R version 3.6.3 was used to analyze the data. The Chi-squared or Fisher's exact test was used to analyze the association of categorical outcomes. Normalized continuous data were compared using the students' t-test; non-parametric continuous

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distribution data were compared using the Mann-Whitney U test. A p-value of <0.05 was considered statistically significant.

3. RESULTS

General characteristics

We included 11 patients with proven *Staphylococcus epidermidis* bloodstream infection. The general characteristics of patients are presented in Table 1. Patients were 7 males, with a median age of 67 (60-74) years, and 4 females, with a median age of 67 (60-74) years. Most patients were bronchial carcinoma (n = 3), and the second most patients were Hodgkin's lymphoma (n=2).

S. epidermidis was isolated from 11 individual Vietnamese cancer patients of whom 02 had Hodgkin's lymphoma, 01 had Esophageal carcinoma, 03 had Bronchial and lung carcinoma, 01 had Hepatocellular carcinoma, and Intrahepatic cholangiocarcinoma, 01 had Colon carcinoma, 01 had Gastric carcinoma, 01 had Rectal carcinoma, and 01 had Breast carcinoma.

Antibiotics resistance pattern

Antimicrobial susceptibility testing results of *Staphylococcus epidermidis* are presented in Table 2 and the antibiotics-resistant profile of *Staphylococcus epidermidis* are presented in Figure 1. All isolates of *S. epidermidis* were resistant to benzylpenicillin and oxacillin, and all of them were multidrug resistant. The 7/11 isolates were resistant to clindamycin, erythromycin, and Trimethoprim-sulfamethoxazole. Methicillin resistance was detected in 4/11 of all isolates (Figure 2).

All isolates of *S. epidermidis* were sensitive to vancomycin, nitrofurantoin, linezolid, and Quinupristin-dalfopristin; 10 isolates were sensitive to tigecycline, 7 isolates were sensitive to rifampicin, and 6 isolates were sensitive to ciprofloxacin, levofloxacin, moxifloxacin.

4. DISCUSSION

To our knowledge, this is the first study in Tan Trieu National Cancer Hospital to document *S. epidermidis* septicemia among Vietnamese cancer patients.

S. epidermidis is one of the noteworthy pathogens that cause bloodstream infections in cancer patients, and the emergence of multi-drug resistance *S. epidermidis* is a cause of concern (2). This study reported the antimicrobial resistance profiles of *S. epidermidis* from blood culture isolates during 4 years. Such data has not previously been reported in Vietnam. The result showed that *S. epidermidis* is responsible for bloodstream infections in Vietnamese cancer patients, which is consistence with previously reported (2). A total of 11 isolates were collected at an average rate of 3 isolates per year which is lower than that in another study that *S. epidermidis* was the most frequently isolated organism at an average rate of 7 isolates per year, from 2010 through 2013 (5).

Resistance to antibiotics has rapidly increased in recent years, and multi-drug-resistant pathogens have become an issue, especially in cancer patients (6). In our study, a high level of methicillin resistance (Figure 2) and resistance to benzylpenicillin and oxacillin, and multi-drug resistance were seen.

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S. epidermidis resistant to rifampicin is a major problem. Thus, various antibiotics, e.g. quinolone, clindamycin, and linezolid have been proposed to be combined with rifampicin to reduce the rate of rifampicin resistance. Furthermore, some recent antibiotics, e.g. daptomycin, tigecycline, and dalbavancin, may be suitable for the treatment of biofilm-producing bacteria such as *S. epidermidis* (7). However, in the present study, *S. epidermidis* resistant to these antibiotics, e.g., rifampicin, quinolone, clindamycin, and tigecycline and that is a growing concern.

In the present study, all of *S. epidermidis* isolates are resistant to penicillin and oxacillin, which is in line with the previous study (8) but higher than that in another study (5). A study conducted in Iran showed that *S. epidermidis* isolated from cancer patients was completely susceptible to clindamycin which is inconsistent with our result that 7/11 isolates were resistant to this antibiotic, which is growing concern.

The high level of methicillin and multidrug resistance of *S. epidermidis* limited the therapeutic options in Vietnamese cancer patients, leading to the costs significantly increasing due to prolonged hospitalization, long-term antimicrobial treatment, morbidity, and mortality.

According to our study, the result showed no resistance to vancomycin, nitrofurantoin, linezolid, and quinupristin-dalfopristin similar to many studies conducted in different countries (2, 6). Another study showed that *S. epidermidis* was the leading cause of bloodstream infection in cancer patients and the occurrence of vancomycin-resistant *S. epidermidis*. That is also worrying although the occurrence of vancomycin-resistant *S. epidermidis* is rare (5).

Vietnamese cancer patients who experience bloodstream infection may have poor outcomes, especially when infected with multi-drug resistant *S. epidermidis*. Stewardship programs that focus on the antibiotics' utility to reduce the abuse of antibiotics should be implemented in Tan Trieu National Cancer Hospital.

5. CONCLUSION

Increased awareness of the pathogenic potential of *S. epidermidis* in Vietnamese cancer patients is required. Vancomycin, nitrofurantoin, linezolid, and quinupristin-dalfopristin are effective antimicrobial agents in treating *S. epidermidis* septicemia in Vietnamese cancer patients. This knowledge is essential for empirical antimicrobials, was defined as the medication prescribed after taking the blood culture and were chosen according to the risk factors of the patients, and clinical manifestations. Plus, selective antibiotics based on local epidemiologic data are significant.

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TABLES AND FIGURES

Table 1. Baseline characteristics of Vietnamese cancer patients.

Characteristic	Overall	Female	Male	p-value[2]
	N = 11[1]	N = 4[1]	N = 7[1]	
Diagnosis				>0.9
Breast carcinoma	1 (9.1%)	1 (25%)	0 (0%)	
Bronchial and lung carcinoma	3 (27%)	1 (25%)	2 (29%)	
Colon carcinoma	1 (9.1%)	0 (0%)	1 (14%)	
Esophageal carcinoma	1 (9.1%)	0 (0%)	1 (14%)	
Gastric carcinoma	1 (9.1%)	0 (0%)	1 (14%)	
Hepatocellular carcinoma and Intrahepatic cholangiocarcinoma	1 (9.1%)	0 (0%)	1 (14%)	
Hodgkin's lymphoma	2 (18%)	1 (25%)	1 (14%)	
Rectal carcinoma	1 (9.1%)	1 (25%)	0 (0%)	
Age	65 (53, 73)	53 (49, 63)	67 (61, 74)	0.11
Unit				>0.9
Intensive care unit	4 (36%)	1 (25%)	3 (43%)	
Internal medicine unit	4 (36%)	2 (50%)	2 (29%)	
Surgery unit	3 (27%)	1 (25%)	2 (29%)	

[1] n (%); Median (Q1, Q3).

[2] Fisher's exact test; Wilcoxon rank sum test.

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Table 2. Antimicrobial susceptibility testing results of *Staphylococcus epidermidis.*

Antibiotics	Antimicrobial susceptibility testing results											Resistant (number)	Sensitive (number)	Intermediate (number)
Benzylpenicillin	R	R	R	R	R	R	R	R	R	R	R	11	0	0
Oxacillin	R	R	R	R	R	R	R	R	R	R	R	11	0	0
Gentamicin	I	S	S	S	R	I	I	I	R	R	R	4	3	4
Ciprofloxacin	S	S	R	S	R	R	S	S	R	S	I	4	6	1
Levofloxacin	S	S	R	S	R	R	S	S	R	S	I	4	6	1
Moxifloxacin	S	S	R	S	R	I	S	S	R	S	I	3	6	2
Clindamycin	R	R	R	S	S	R	R		R	R	S	7	3	0
Erythromycin	R	R	R	S	S	R	S	R	S	R	R	7	4	0
Quinupristin-dalfopristin	S	S	S	S	S	S	S	S	S	S	S	0	11	0
Linezolid	S	S	S	S	S	S	S	S	S	S	S	0	11	0
Vancomycin	S	S	S	S	S	S	S	S	S	S	S	0	11	0
Tetracycline	R	S	R	S	R	R	S	R	S	R	S	6	5	0
Tigecycline	R	S	S	S	S	S	S	S	S	S	S	1	10	0
Nitrofurantoin	S	S	S	S	S	S	S	S	S	S	S	0	11	0
Rifampicin	S	R	S	R	S	S	S	R	S	S	R	4	7	0
Trimethoprim-sulfamethoxazole	R	S	R	R	S	R	R	S	S	R	R	7	4	0

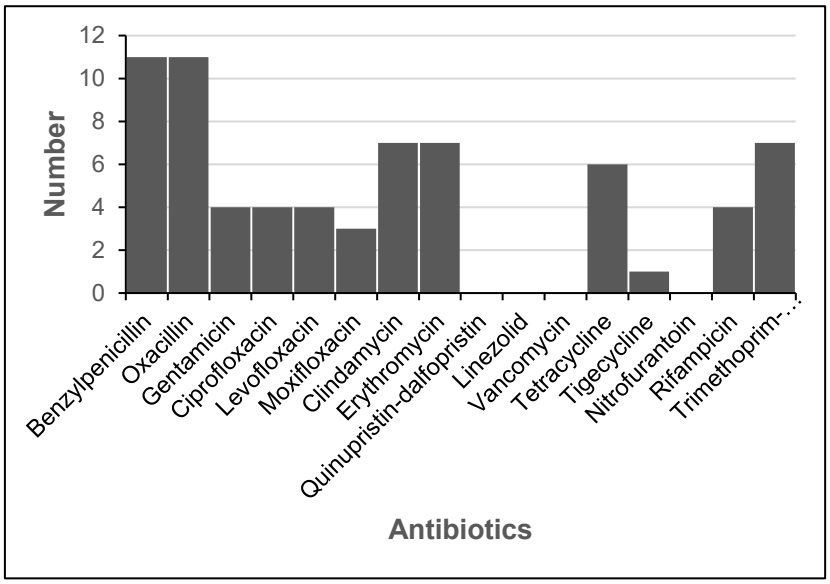

Figure 1. Antibiotic resistance profile of *Staphylococcus epidermidis*

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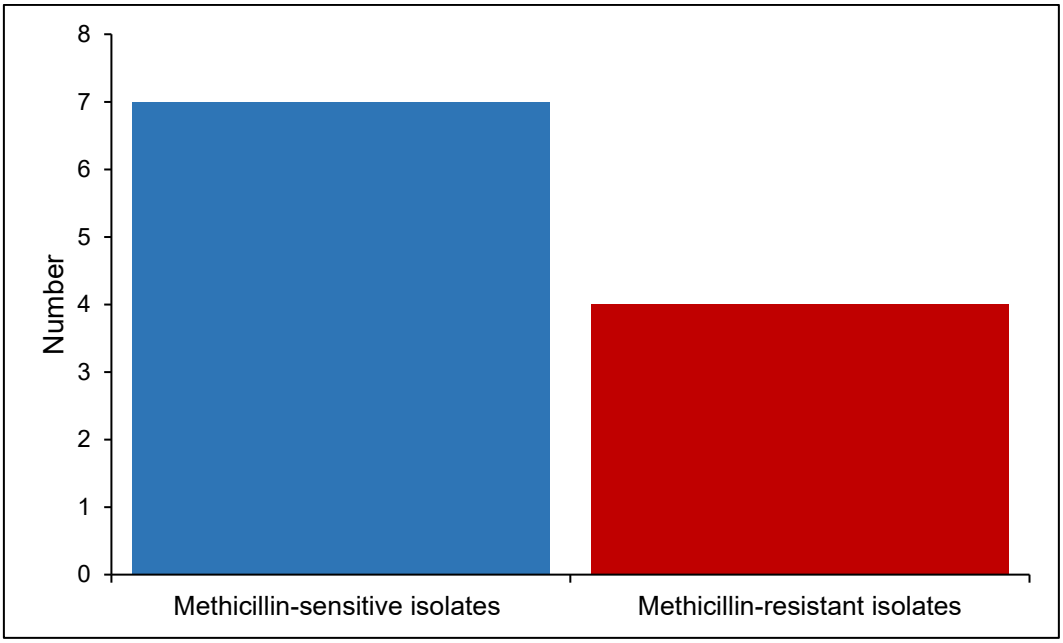

Figure 2. Methicillin resistance profile of *Staphylococcus epidermidis*