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Characteristic of Bacterias and Antibiotic Sensitivity of Blood Culture in Sepsis

Jesica Sidabutar[1], Nurmalia Purnama Sari[2*], Phey Liana[2]

[1] Undergraduate Programme, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
[2]Department of Clinical Pathology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

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Corresponding author:
Nurmalia Punama Sari

E-mail address:

nurmaliaps31@gmail.com

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ABSTRACT

Background: Sepsis is a group of symptoms caused by infection, characterized by organ dysfunction due to compromised hosts response to infection hence may lead to a life-threatening condition. One of the treatments for sepsis stated in one hour-bundle is the administration of broad-spectrum antibiotics before the culture results obtained. Improper use of antibiotics may lead to antibiotic resistance. The purpose of this study was to describe the microbes pattern and their sensitivity to antibiotics in patients with sepsis at Muhammad Hoesin Hospital, Palembang, to contribute to a useful treatment guideline and to provide a reference for further research. **Methods:** This study was a descriptive observational study with a cross-sectional design using medical record of patients diagnosed with sepsis whose blood culture results were positive. This study was conducted at Muhammad Hoesin Hospital, Palembang, from January 2017 to December 2018. The data was processed and analyzed by univariate analysis using the SPSS 21.0 computer program. **Results:** The study subjects were predominantly children with Gram-positive bacteria (24.6%) as the most common cause. The most common bacteria observed were *Staphylococcus epidermidis* (35.7%), *Staphylococcus aureus* (27.3%), *Staphylococcus haemolyticus* (24%), and *Staphylococcus hominis* (21.4%). Linezolid (100%), nitrofurantoin (100%), and quinupristin/dalfopristin (100%) were found to be sensitive to gram-positive bacteria. **Conclusion**: Gram-positive bacteria were the most common cause of sepsis in Muhammad Hoesin Hospital, Palembang. The bacteria were sensitive to linezolid, nitrofurantoin, and quinupristin/ dalfopristin.

1. Introduction

Sepsis is a group of symptoms caused by infection, identified from clinical signs The 3rd International Consensus Definition for Sepsis and Septic Shock (Sepsis-3) 2016 defined sepsis as a dysfunction due to compromised host response regulation to infection hence may lead to life-threatening conditions.[1] Organ dysfunction in patients with suspected sepsis can be assessed using the quick Sequential Organ Failure Assessment (qSOFA), consisting of respiratory rate ≥ 22x / minute, mental status alteration, and systolic blood pressure ≤ 100 mmHg.[1,2] qSOFA ≥ 2 indicates organ dysfunction, but this cut-off is not very sensitive.[2]

A study from the Global Burden Disease in 2017 revealed that there were around 48.9 million cases of sepsis worldwide with a mortality rate up to 11 million cases (19.7% of the worldwide deaths).[3] A study conducted in Southeast Asia from 2013- 2015 showed that sepsis patients were predominantly aged ≥ 18 years (51.6%) and were male (56.7%).[4] There is no data on national sepsis patients yet, but medical record data for the 2017-2018 period at Mohammad Hoesin Hospital showed that around 321 patients were diagnosed with sepsis. The most common sources of infection that may lead to sepsis were acute respiratory infections, followed by acute systemic infections, acute diarrhoea, and central nervous system infections.[4] Intensive Care Over Nations revealed that gram-negative bacteria were the most common aetiology for sepsis.[5]

One of the treatments recommended by The Surviving Sepsis Campaign Bundle in 2018 in “hour-1 bundle” was the administration of broad-spectrum antibiotics before culture results obtained. Inappropriate antibiotics administration leads to antibiotic resistances as observed in Adam Malik Hospital in 2016, where Amikacin, Meropenem, Cefoperazone Sulbactam, and Vancomycin showed a high level of resistance.[7] The increase in antibiotic resistance is caused by several factors, such as the mechanism of the bacteria to survive, nosocomial infections from other patients with resistant bacterial infections, the inappropriate use of antibiotics, and implementation of monotherapy that decreases the potency of antibiotics.[8]

Understanding the pattern of microbes and their sensitivity to antibiotics in patients with sepsis is essential for successful therapy. However, there are no studies conducted to address the issue yet. This study was aimed to describe the characteristic of microbes and their sensitivity to antibiotics in patients with sepsis.

2. Methods

This study was a descriptive observational study with a cross-sectional design, conducted from September to December 2019 at the Clinical Microbiology Laboratory of Mohammad Hoesin Hospital, Palembang. The subjects were of patients with sepsis with available blood culture results at the Clinical Microbiology Laboratory of Mohammad Hoesin Hospital Palembang from January 2017 to December 2018. Total sampling was applied, all patients diagnosed with sepsis with the complete medical record, including a positive blood culture result for bacteria, were included.

Observed characteristics were age, gender, inpatient room, types of bacteria, antibiotics, and sensitivity test. Data were processed and analyzed with univariate analysis using the SPSS 21.0 computer program to obtain the distribution and percentage of each studied variables.

3. Results

A total of 102 patients, consisted of 57 people in 2017 and 45 subjects in 2018, met the inclusion criteria. In 2017, 18 patients were positive for bacteria, with the most common cause of gram-positive bacteria (24.6%). Meanwhile, in 2018, 20 subjects were positive for bacteria, with the most common cause of gram-positive bacteria (24.4%). In 2017, the issues were predominantly children (45.6%) and were male (68.4%). Meanwhile, in 2018, the subjects were mainly children (46.7%) and were female (55.6%). Demographic characteristics are described in **Tables 1 and 2.**

In hospital wards, gram-positive bacteria were mostly observed in the Selincah 1-2-3 (pediatric room) in 2017 and 2018, while gram-negative bacteria were primarily observed in High Care Unit (HCU) in 2017 and Pediatric Intensive Care Unit (PICU) in 2018 **(Table 3).**

The most common Gram-positive bacteria leading to sepsis were *Staphylococcus sp.*, while the most common Gram-negative bacteria leading to sepsis were *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. The list of bacteria can be seen in **Table 4 and 5.**

Antibiotic sensitivity tests to Gram positive bacteria in 2017 revealed sensitivity to Amikacin (66.7%), Gentamicin (54.5%), Linezolid (75%), Moxifloxacin (100%), Tetracycline (75%), Tigecycline (100%), and Vancomycin (72.7%), while in 2018 Linezolid (100%), Nitrofurantoin (100%), Quinupristin/Dalfopristin (100%), Tetracycline (66.7%), Tigecycline (100%), Trimethroprim / Sulfamethoxazole (66.7%), and Vancomycin (100%) were revealed to be sensitive **(Figure 1 and 2).**

Gram-negative bacteria sensitivity test in 2017 revealed sensitivity to Amikacin (100%), Trimethoprim / Sulfamethoxazole (100%), and Vancomycin (100%), similar to sensitivity test in 2018 **(Figure 3 and 4).**

Table 1. Characteristics of patients with sepsis and microbes leading to sepsis in Palembang

Characteristics	2017	2018
Blood specimens of patients with sepsis	57 (55.9%)	45 (44.1%)
N = 102		
Grown	18 (31.6%)	20 (44.4%)
Sterile	39 (68.4%)	25 (55.6%)
Bacteria that cause sepsis		
Gram-positive bacteria	14 (24.6%)	11 (24.4%)
Gram-negative bacteria	4 (7%)	9 (20%)
Gender		
Male	39 (68.4%)	20 (44.4%)
Female	18 (31.6%)	25 (55.6%)

Table 2. Distribution of patients with sepsis by age

Age Group	2017 (N=57)		2018 (N=45)	
	n	%	n	%
Children (0-11 years old)	26	45.6	21	46.7
Adolescent (12-25 y.o.)	4	7	3	6.7
Adult (26-45 y.o.)	2	3.5	3	6.7
Elderly (46-65 y.o.)	12	21.1	11	24.4
Senescent (≥ 66 y.o.)	13	22.8	7	15.6

Table 3. Bacteria leading to sepsis in hospital wards

Hospital Wards	2017				Sterile		2018				Sterile	
	Gram Positive Bacteria		Gram Negative Bacteria				Gram Positive Bacteria		Gram Negative Bacteria			
	n	%	n	%	n	%	n	%	n	%	n	%
High care unit (HCU)	3	21.4	2	50	5	12.8	1	9.1	0	0	2	8
Emergency unit transferred	2	14.3	0	0	1	2.6	1	9.1	1	11.1	2	8
Graha operating room transferred; 3rd Floor	0	0	0	0	1	2.6	-	-	-	-	-	-
Selincah 1-2-3 (pediatric room)	6	42.9	1	25	10	25.6	6	54.5	3	33.3	6	24
Selincah (Neonates)	1	7.1	1	7.7	2	3.1	0	0	1	11.1	2	8
Kelingi 1.1	-	-	-	-	-	-	0	0	0	0	2	8
Kelingi 1.2	-	-	-	-	-	-	0	0	0	0	1	4
Kelingi 2.2	-	-	-	-	-	-	0	0	0	0	1	4
Rawas 1.1	0	0	0	0	1	2.6	-	-	-	-	-	-

Rupit 1.2	0	0	0	0	1	2.6	0	0	0	0	1	4
Komering 1.1	0	0	0	0	1	2.6	1	9.1	0	0	0	0
Komering 1.2	1	7.1	0	0	4	10.3	1	9.1	0	0	4	16
Musi 1.1 / 1.2	0	0	0	0	1	2.6	0	0	0	0	1	4
Musi 2.1 / 2.2	0	0	0	0	2	5.1	-	-	-	-	-	-
Ogan	0	0	0	0	1	2.6	1	9.1	0	0	1	4
Lakitan 1.3	-	-	-	-	-	-	0	0	0	0	1	4
NICU	0	0	1	25	1	2.6	-	-	-	-	-	-
PICU	0	0	0	0	7	17.9	0	0	4	44.4	1	4
GICU	0	0	0	0	3	7.7	-	-	-	-	-	-
HCU (BHC)	1	7.1	0	0	0	0	-	-	-	-	-	-
Total	14	100	4	100	39	100	11	100	9	100	25	100

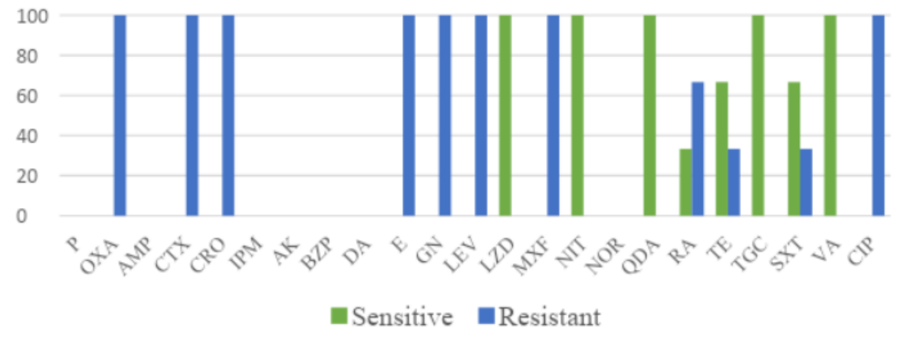
Table 4. Distribution of gram-positive bacteria Leading to Sepsis

No	**Bacteria**	**2017**		**2018**	
		n	**%**	**n**	**%**
1	*Staphylococcus epidermidis*	5	35.7	0	0
2	*Staphylococcus haemolyticus*	3	21.4	3	27.3
3	*Staphylococcus hominis*	3	21.4	0	0
4	*Staphylococcus capitis*	1	7.1	1	9.1
5	*Enterococcus faecalis*	1	7.1	0	0
6	*Staphylococcus saprophyticus*	1	7.1	0	0
7	*Staphylococcus aureus*	0	0	3	27.3
8	*Staphylococcus hominis ssp hominis*	0	0	3	27.3
9	*Streptococcus parasanguinis*	0	0	1	9.1
	Total	**14**	**100**	**11**	**100**

Table 5. Distribution of gram-negative bacteria leading to sepsis

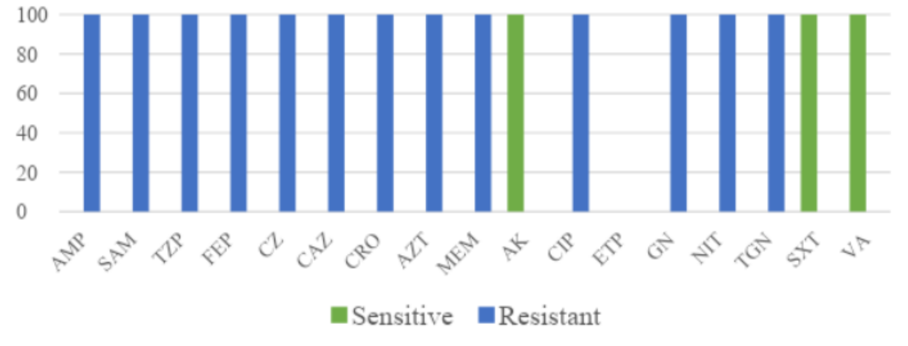
No	**Bacteria**	**2017**		**2018**	
		n	%	n	%
1	*Pseudomonas aeruginosa*	1	25	2	22.2
2	*Acinetobacter baumannii*	1	25	2	22.2
3	*Escherichia coli*	0	0	2	22.2
4	*Burkholderia cepacian*	0	0	1	11.1
5	*Klebsiella pneumoniae ssp pneumoniae*	0	0	1	11.1
6	*Sphingomonas paucimibilis*	0	0	1	11.1
7	*Acinetobacter baumannii/calcoaceticus*	1	25	0	0
8	*Enterobacter cloacae*	1	25	0	0
	Total	**4**	**100**	**9**	**100**

Figure 2. Gram Negative Bacteria Sensitivity Test in 2018



Grafik 2. Data Sensitivitas Bakteri Gram Positif Tahun 2018

Figure 3. Gram Negative Sensitivity Test in 2017



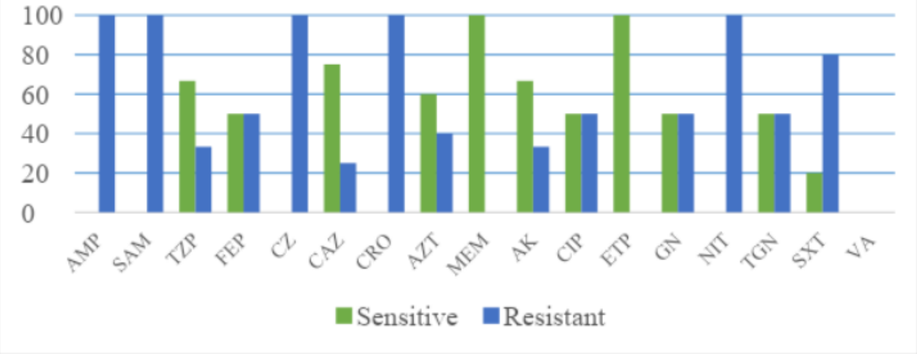


Figure 4. Gram Negative Sensitivity Test in 2018

4. **Discussion**

Demographic characteristics revealed that patients with sepsis in 2017 and 2018 were predominantly children (0-11 years). This result is in line with a study in Southeast Asia, revealing a predominant age group of ≥ 1 year to <5 year old among patients with sepsis.[4] Another survey conducted in PICU of Sanglah Hospital Bali also confirmed the incidence of sepsis in neonates and infants with the primary source of infection the respiratory tract and community-acquired infection.[9] However, a contradictive result was exhibited by a study conducted in PICU of Mohammad Hoesin Hospital Palembang, stating that hospital infections were higher than community infections (95.8%).[10]

Patients with sepsis in 2017 were predominantly male (68.4%), while in 2018 patients with sepsis mostly female(55.6%). The mortality rate for sepsis in 2017 at Mohammad Hoesin Hospital Palembang was higher for male (63.2%). These results were consistent with a study conducted in Wahidin Sudirohusodo Hospital Makassar reporting predominant sex of male among patients with sepsis (69.8%).[11] Another survey at a hospital in Bandung stated that sepsis was most commonly observed in female patients.[12] Relationship between sex and risk for mortality depends on the individual immune response. However, women produce a higher level of estrogen than men resulting in better immune system activity.[12]

The most common bacteria observed in sepsis in Mohammad Hoesin Hospital Palembang were Gram-positive bacteria consisting of *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Staphylococcus aureus*, and *Staphylococcus hominis*. These results are in line with a study conducted in Moewardi Hospital, stating that the most common cause of sepsis were Gram-positive bacteria (65.9%).[13] Another survey conducted in North-Western Ethiopia said that coagulase-negative staphylococcus (CoNS) and *Staphylococcus aureus* were the most common bacteria observed in blood culture of patients with sepsis.[14] CoNS is a common bacteria observed in nosocomial bacteremia due to the increased use of medical devices, including intravenous catheters, vascular grafts, prosthetic heart valves and tools used in the treatment of joint disease.[12] The presence of CoNS in blood cultures cannot directly determine that the species is pathogenic, because 85% of CoNS isolates were found to be contaminants.[12] Majority of *Staphylococcus sp.* present as normal flora in human skin and mucous membranes, however, they have virulence factors that may increase the efficacy and infection, strong acids and adhesion factors that may lead to avoidance of host defence as an enzyme (staphylokinase) and then spread (hyaluronidase).[15]

Majority of Gram-positive bacteria in 2017 were resistant to Penicillin G, Ampicillin, and Ceftriaxone, while sensitive to Moxifloxacin, Linezolid, and Norfloxacin. In 2018, the highest sensitivity levels for Gram-positive bacteria were Linezolid, Nitrofurantoin, and Quinupristin/ Dalfopristin. These results were in line with a study conducted in Moewardi Hospital stated that Gram-positive bacteria leading to sepsis were sensitivity to Linezolid and Moxifloxacin.[13] Another study said that Gram-positive bacteria resistant to penicillin-G, erythromycin, and trimethoprim-sulfamethoxazole, which is an empirical therapy for *Staphylococcus sp* infection.[14] Based on sensitivity test in Gram-positive bacteria, there were three bacteria identified to be MDRO, namely *Staphylococcus epidermidis, Staphylococcus haemolyticus*, and *Staphylococcus hominis*. MDRO is defined as bacterial resistant to at least one antibiotic from more than three drug classes.[16] These results were supported by a study Batara in exhibited that the three MDR bacteria were more resistant to class A antibiotics. Class A antibiotics are common antibiotics used for certain groups of organisms, including ampicillin, cephazolin, gentamycin, and piperacillin/tazobactam.[17]

Gram-negative bacteria in 2017 were observed to be sensitive to amikacin, trimethoprim/sulfamethoxazole, and vancomycin, while gram-negative bacteria in 2018 were honoured to be sensitive to piperacillin/tazobactam, aztreonam, meropenem. These results are consistent with other studies conducted at Cipto Mangunkusumo Hospital exhibiting carbapenem (imipenem, meropenem, doripenem) sensitive gram-negative bacteria.[18] Gram-negative bacteria resistance is caused by several mechanisms, including the production of enzymes to compromise antibiotics by hydrolysis or DNA gyrase and DNA topoisomerase IV mutation and capability to modify antibiotics such as observed in *Acinetobacter spp*. which capable of inactivating antibiotics using enzymes, prevent antibiotics from reaching their targets, and target mutations of antibiotics.[13] Based on the results of the Gram-negative bacteria sensitivity test, there were three bacteria identified to be MDRO, namely *Pseudomonas aeruginosa, Acinetobacter baumanni*, and *Escherichia coli*.

The results of this study also showed a high level of sterile blood cultures, 39 cases (68.4%) in 2017 and 25 patients (55.6%) in 2018. This condition is affected by several factors, such as blood sampling conducted in > 6 hours from admission, frequent withdrawals with a volume <10 ccs, the use of 2 kinds of antiseptics before the blood-taking procedure, and the time lag between antiseptic and blood drawing of > 30 seconds.[19]

5. Conclusion

Patients with sepsis in Palembang were predominantly children (0-11 years old) and male gender. Gram-positive bacteria are the most common bacteria observed in pediatric ward, including *Staphylococcus epidermidis, Staphylococcus aureus, Staphylococcus haemolyticus*, and *Staphylococcus hominis,* that were still sensitive to linezolid, nitrofurantoin, and quinupristin/dalfopristin.

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