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The Bacterial Profile and Antimicrobial Susceptibility Pattern among Patients with Suspected Bloodstream Infection in Universitas Sumatera Utara Hospital, Indonesia

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Abstract: *Bloodstream infection is a health problem that causes morbidity and mortality worldwide, more thought is the problem of antimicrobial resistance so that the choice of therapy becomes difficult and limited. This study aims to determine the bacterial profile and antimicrobial sensitivity pattern that can be used as a basis for choice effective antimicrobial therapy in the treatment of bloodstream infections. A retrospective study was conducted from January to August 2019 with a total of 300 patients with suspected blood infections in USU Hospital Medan, Indonesia. Blood samples in the Microbiology Laboratory using the BacT/ALERT, identification and antimicrobial sensitivity testing using Vitek 2 Compact. The results showed that gram-positive bacteria had a higher percentage (65.3%) than gram-negative bacteria (34.7%). The dominant bacteria that cause bloodstream infections are S. aureus (31%), followed by S. epidermidis (14%) and P. aeruginosa (12%), E. faecalis (6%), M. luteus (6%), K. pneumoniae (6%),A. baumannii(6%), P. vulgaris (4%), K. kristinae(4%), P. mirabilis (2%), E. coli (2%), E. aerogenes (2%), S. coagulase-positive (2%), and S. α-haemolyticus(2%). Vancomycin is the only antibiotic that has 100% sensitivity to all gram-positive bacteria. Whereas in gram-negative, antibiotics with >80% percentages such as levofloxacin, amikacin, and meropenem can be recommended as definitive therapies especially for cases of multiple-drug resistantorganisms.*
Keywords: *Bloodstream infection, Antimicrobial Pattern, MDROs*

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I. Introduction

Bloodstream infections are still a serious cause of infection which can cause morbidity and mortality among hospitalized patients worldwide[1]. This problem is still a burden for hospitals, where the spectrum of microorganisms has expanded and can change geographically. Indonesia is a country that has a high burden. In addition to bacterial infections, a problem that concerns the world is the emergence of antimicrobial resistance[2]. Bloodstream infections require fast and aggressive antimicrobial treatment[3,4]. The choice of antimicrobial for infections caused by resistant microorganisms is difficult because it requires treatment with more expensive antibiotics, which of course can stop treatment in hospitals and increase the risk of death[2]. In the most basic cases, existing antimicrobials are formally initiated separately from the available blood culture results. Given the high mortality and morbidity associated with septicemia, the choice of appropriate empirical therapy is very important[5].

Blood culture is a gold standard technique that provides important information for proper diagnosis and treatment to obtain infectious bacteria and definitive therapy, thus saving the lives of patients with bloodstream infections, bacteremia, and septicaemia[2,5,6]. Therefore, this study aims to analyze various microorganisms that cause blood flow infections and antimicrobial sensitivity patterns, because it will be a guideline for doctors who start special antibiotic therapy. It is important to remember that each hospital has a different bacterial profile and antimicrobial sensitivity pattern.

II. Material and Methods

Study Design, Area and Population

A descriptive cross-sectional study was conducted in the period from January to August 2019 based on records of culture and antibiotics susceptibility test results of blood in the Clinical Microbiology Laboratory, Universitas Sumatera Utara Medan, Indonesia. A total of 300 samples from clinically suspected cases of bacteremia.

Sampling technique and Bacterial Culture

All the samples were collected from indoor patients in our hospital during the study period and processed in the Clinical Microbiology Laboratory. Blood was collected from vena, in adult cases avg. 8 mL aseptically and inoculated immediately into BacT/ALERT FA plus-aerobic blood culture bottles and pediatric cases 1-2mL of blood was inoculated in BacT/ALERT PF plus pediatric blood culture bottles. After collection, these bottles were immediately incubated in BacT/ALERT 3D a fully automated blood culture system for detection of growth in blood culture. Negative results are released after the 5th day, while positive results will automatically give a warning sign, the positive bottle is then cultivated on routine Blood Agar and Mac-Conkey Agar, incubated for 24 hours at 37^{o}C.

Colonies that grew on the surface of the media were followed by gram staining, then identification of bacteria was used by the Vitek ID card and the antibiotic sensitivity test was used by the AST Vitek Card. Automatically, the Vitek 2 Compact tool will identify the type of bacteria and antibiotic sensitivity is based on the CLSI 2018 standard.

Data analysis

All the results collected were subjected to descriptive statistics like mean and percentages. Microsoft Excel was used for making tables, and calculations.

III. Results

Blood culture is a well-established procedure of the standard diagnostic workup for bloodstream infections. During the study period, 300 blood cultures were analyzed in which 49 of them showed positive cultures. The overall prevalence of blood culture positive of bacteremia suspected patients was 49/300 (16%). Among 49 positive cultures, were 32 (65.3%) Gram-positive bacteria and 17 (34.7%) Gram-negative bacteria. The distribution and percentage of various bacteria are shown in Table 1.

Table 1. Distribution of recovered bacteria from blood cultures

Microorganisms (n=49) No.(%)	Type	No. (%)
Gram-positive bacteria 32 (65.3)	*Staphylococcus aureus*	15 (31)
	Staphylococcus epidermidis	7 (14)
	Enterococcus faecalis	3 (6)
	Micrococcus luteus	3 (6)
	Kocuriakristinae	2 (4)
	Staphylococcus coagulase-positive	1 (2)
	Streptococcus α-haemolyticus	1 (2)
Gram-negative bacteria 17 (34.7)	*Pseudomonas aeruginosa*	6 (12)
	Klebsiella pneumoniae	3 (6)
	Acinetobacter baumannii	3 (6)
	Proteus vulgaris	2 (4)
	Proteus mirabilis	1 (2)
	Escherichia coli	1 (2)
	Enterobacter aerogenes	1 (2)

From table 1, it can be seen that gram-positive bacteria have a higher percentage of 65.3%, where *S. aureus* is the most pathogenic bacteria found as a cause of bloodstream infection with a growth percentage of 15/49 (31%). This study consistent with previous studies in Ethiopia, where the dominant is 127/164 (77.4%) gram-positive with the most *S. aureus* 82/127 (50%)[7]. In India it's 39/75 (52%) gram-positive which is dominated by *Staphylococcus aureus*[8] and Denpasar-Bali, Indonesia 50%[9]. This study is different from research in Iran, where the dominant bacteria are the gram negative group (55.4%) such as *Pseudomonas sp*., *Klebsiella sp*. and *Acinetobacter sp*.[10]. In India are 161/299 (53.8%) gram-negative bacteria such as *Escherichia coli* (37.80%) were found to be most predominant followed by *Klebsiella sp.* (24.20%), *Pseudomonas sp.* (13.60%) and *Acinetobacter* sp. (6.80%)[11]. This difference can be due to geographic location, epidemiology in etiological agents, variations in culture systems, and research designs.

The second most Gram-positive type of bacteria after *S. aureus* is *S. epidermidis* 7 (14%), then followed by 3 (6%) *E. faecalis*, 3 (6%) *M. luteus*, 2 (4%) *K. kristinae*, 1 (2%) *S.coagulase-positive* and 1 (2%) *S. α-haemolyticus*. In this study the percentage of gram-negative bacteria was 17/49 (34.7%), with the most types of bacteria being *P. aeruginosa* 6 (12%), followed by *K. pneumonia* 3 (6%), 3 (6%) *A. baumannii*, 1 (2%) *P. vulgaris*, 1 (2%) *P. mirabilis*, 1 (2%) *E.coli*, and (2%) *E. aerogenes*. The antibiotic susceptibility patterns of Gram-positive bacteria are shown in Table 2 and those of Gram-negative bacteria are shown in Table3.

Table 2. Antibiotic susceptibility pattern of Gram-positive bacteria.

Gram-positivebacteria	Antimicrobial Susceptibility Pattern (%Susceptible)														
	AMP	AML	FOX	CTX	CAZ	CRO	C	CIP	DA	SXT	TE	E	GN	MEM	VA
S. aureus (15)	20	20	20	20	20	20	33	20	60	67	53	40	20	20	100
S.epidermidis(7)	14	14	14	14	14	14	43	14	14	71	43	14	14	14	100
E.faecalis(3)	0	0	-	0	0	0	0	0	0	0	33	0	0	-	100
M. luteus (3)	67	67	-	67	67	67	67	67	67	67	100	67	67	-	100
K.kristinae(2)	0	0	-	100	100	100	100	50	50	50	100	50	50	-	100
S.α-haemolyticus(1)	0	0	-	100	100	100	100	0	0	0	0	100	-	-	100
S. cog-positive (1)	100	100	100	100	100	100	100	100	100	0	0	100	100	100	100

Table 2 shows that *S. aureus*, *S. epidermidis* and *E. faecalis* have a low sensitivity to ampicillin, amoxicillin, cefoxitin, cefotaxime, ceftazidime, ceftriaxone, chloramphenicol, ciprofloxacin, clindamycin, cotrimoxazole, tetracycline, erythromycin, gentamycin, and meropenem with the percentage <80%. While *M. luteus* has a 67% sensitivity to ampicillin, amoxicillin, cefotaxime, ceftazidime, ceftriaxone, chloramphenicol, ciprofloxacin, clindamycin, cotrimoxazole, erythromycin, and gentamycin. In *K. kristinae*and *S.α-haemolyticus*there is 100% sensitivity to cefotaxime, ceftazidime, ceftriaxone, chloramphenicol, tetracycline, and vancomycin. In *Staphylococcus coagulase-positive* only cotrimoxazole and tetracycline are resistant to this isolate. All gram-positive bacteria isolates were found to be sensitive to vancomycin.

Table 3. Antibiotic susceptibility pattern of Gram-negative bacteria.

Gram-negative bacteria	Antimicrobial Susceptibility Pattern (%Susceptible)														
	AK	SAM	AMC	ATM	CTX	CAZ	CRO	FEP	SCF	CIP	SXT	TE	GN	LEV	MEM
P. aeruginosa (6)	83	17	0	0	17	67	0	67	67	67	67	50	17	83	50
K. pneumonia (3)	33	0	0	0	0	0	0	0	67	0	0	0	0	100	67
A. baumannii(3)	100	100	33	33	33	33	33	33	100	33	67	33	33	33	100
P. vulgaris (2)	50	50	50	50	50	50	50	100	50	50	0	0	0	100	100
P. mirabilis (1)	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
E. coli (1)	0	0	0	0	0	0	0	100	0	100	0	100	0	100	100
E. aerogenes (1)	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100

Table 3 shows that only amikacin and levofloxacin have >80% sensitivity to *P. aeruginosa*. Only levofloxacin is sensitive >100% to *K. pneumoniae*. Whereas *A.baumannii*has a 100% percentage of amikacin, ampicillin/sulbactam, cefoperazone/sulbactam, and meropenem. Only cefepime and meropenem have 100% sensitivity to *P. vulgaris*. In *E. coli* there are 100% sensitive percentages of cefepime, ciprofloxacin, tetracycline, levofloxacin, and meropenem. All antibiotics are sensitive to *P.mirabilis*and *E. aerogenes*. The isolates of multiple-drug resistant organisms are found in the following table4.

Table 4. MDROs pattern of the bloodstream infections.

Type of MDROs	No. (%)
Methicillin resistant Staphylococcus aureus (MRSA)	12/15 (80)
Methicillin resistant Staphylococcus epidermidis (MRSE)	6/7 (85)
Klebsiella pneumoniae Extended Spectrum Beta-Lactamases (ESBls)	3/3 (100)
Pseudomonas aeruginosa Carbapenemase	3/6 (50)
Klebsiella pneumoniae Carbapenemase	1/3 (33)

Table 4 shows that there is a fairly high percentage of MRSA and MRSE, where the isolate found is resistant to all methicillin groups. This resistance becomes a big problem which makes the choice of MRSA and MRSE therapy difficult, where the only last choice drug is vancomycin. Irrational use of antibiotics is responsible for developing a collection of resistant bacteria and negative blood culture results. In countries like Indonesia, where many types of drugs including antibiotics are sold freely[12]. This is also one of the causes of resistance due to microorganisms that cannot be eliminated, will become MDROs candidates.

All *K. pneumoniae* isolates found were ESBLs. This is consistent with previous research, where ESBLs cause resistance to beta-lactam antibiotics such as penicillin, cephalosporins, and monobactams[13] Not as ESBLs, found 1/3 (33%) *K.pneumoniae*isolate is a type of carbapenemase. The only therapeutic option for *K.pneumoniae*ESBLs and *K. pneumoniae carbapenemase*is levofloxacin. Besides, 3/5 (50%) of *P. aeruginosa* isolates are a type of carbapenemase. Amikacin and levofloxacin are the definitive therapies recommended for *P. aeruginosa carbapenemase*because they have a sensitivity of 83%.

In this study, vancomycin was found to be most effective for gram-positive isolates. Whereas Levofloxacin was found to be most effective for gram-negative bacteria, followed by meropenem and amikacin. These four antibiotics should not be used without culture results and are the last resort for the treatment of bloodstream infections. These antibiotics can be kept as reserve drugs because if resistance is developed then treatment will be complicated.

IV. Conclusions

The results of this study indicate that gram-positive bacteria have a higher percentage (65.3%) than gram-negative bacteria (34.7%). The dominant bacteria that cause bloodstream infections are *S. aureus* (31%), followed by *S. epidermidis* and *P. aeruginosa*. Antibiotics with a sensitivity percentage> 80% can be recommended as a definitive therapy, for gram-positive bacteria are vancomycin, while for gram-negative bacteria are levofloxacin, meropemem and amikacin.

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