



Microorganism Spectrum and Its Sensitivity Pattern at Intensive Care Unit of a Secondary Care Teaching Hospital in Tangerang, Indonesia

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Abstract

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BACKGROUND: Antimicrobial resistance is one of the world's problems. It occurs due to misuse of antimicrobials in dealing with infectious diseases, making antimicrobial drugs less effective in treating infectious diseases. Antimicrobial sensitivity pattern is useful for directing clinicians in empirical therapy and preventing antimicrobial abuse so that resistance to antimicrobial drugs does not occur.

AIM: This research is conducted to identify the microorganism spectrum and its sensitivity pattern at the intensive care unit (ICU) of a secondary care teaching hospital in Tangerang, Indonesia.

METHODS: This study is a cross-sectional observational retrospective study done in the ICU of secondary care teaching hospital in Tangerang, Indonesia from January 2019to June 2020. This study used 1,341 isolated extracted from the ICU of a secondary care teaching hospital in the Tangerang database. All the samples would be analyzed using Microsoft Excel 2013 and Statistical Package for the Social Science 25 (SPSS 25) using ANOVA analysis.

RESULTS: From 1,341 isolates, the most common microorganism found was *Klebsiella pneumoniae* 221(16%) and the most common specimen is sputum 905 (67,48%). Gram-negative bacteria had the highest sensitivity to amikacin 62% and imipenem 59%. Gram-positive bacteria had the highest sensitivity to tigecycline 98% and doxycycline 95%. While *Candida* spp. had the highest sensitivity to micafungin (96%) and voriconazole (97%).

CONCLUSIONS: This study showed that the sensitivity of antimicrobials was no longer effective in treating infection. Therefore, the government and doctors must play an important role in socializing the correct way of using antimicrobial.

Introduction

Antimicrobial resistance is one of the most concerning health problems in the world, where antimicrobial resistance occurs due to changes in microorganisms such as bacteria, fungi, viruses, and parasites to the antimicrobial drugs given. This makes antimicrobial drugs less effective in the treatment of an infectious diseases [1].

Antimicrobial resistance usually occurs due to misuse of antimicrobials in dealing with an infectious disease. Antimicrobial abuse can be due to a lack of knowledge regarding the use of antimicrobials, community preference for purchasing antimicrobials, and a lack of policies for regulating the use of antimicrobials. Based research conducted in Pekan Baru, in Sumatra Island, Indonesia showed that the rational use of antimicrobial in intensive care unit (ICU) was 67.7% and some clinicians gave antimicrobial without indications, which was about 8.82%. Some clinicians did not comply with the antimicrobial administration protocol and did not monitor antimicrobial therapy properly, so it caused some classes of antimicrobial to become resistant [2].

Infectious disease is one of the most common diseases in developing countries such as Indonesia. Infection most often occurs in the ICU. This is because patients who are in the ICU are mostly patients with immunosuppression, so they are more susceptible to infection. In addition, a patient who is in the ICU is also in frequent contact with hospital staff, which can cause nosocomial infections [3]. Patients in the ICU are susceptible to acquiring nosocomial infection due to immunocompromised or aseptic error in invasive treatment and secondary infection due to exposure to broad-spectrum antibiotics [4], [5], [6]. The risk factors for patients in ICU getting infected are the use of mechanical ventilators, catheters, and invasive devices for a long time [7]. ICU-acquired infection is an independent factor that determines patient mortality after adjustment for APACHE II score and age (OR 4.0 [95% CI: 2.0-7.9]). The increase in mortality in ICU patients is also due to Gram-negative bacteremia and intra-abdominal infection [4].

Therefore, we have to make a pattern of microorganisms and their sensitivity, so the clinicians can provide appropriate antimicrobial treatment and can reduce the mortality rate of ICU patients. Patterns of microorganisms and their sensitivity can be used for empirical treatment in certain hospitals. Antibiograms are useful for directing clinicians in charge of empirical therapy, while waiting for the culture's results so that resistance to antimicrobial drugs does not occur [8].

Materials and Methods

Study design and setting

This study was a cross-sectional observational retrospective study, where the data used were secondary data taken from the database of microbiology laboratory from ICU of Siloam Teaching Hospital from January 2019 to June 2020.

Inclusion criteria for study population

All isolates from critically ill patients who admitted to ICU, high care unit, and intensive cardiac care unit were included in the study.

Consent to study

A waiver of consent was obtained from the Pelita Harapan University Faculty of Medicine Ethics Committee since the study posed no risk to the patients.

Sampling methods, collection, handling, and processing

The non-probability retrospective sampling was used on the data. Clinical specimens were collected according to the standard protocol for microbiology examination. The blood sample taken is venous blood, where the site of the collection was aseptic with 70% alcohol. Blood can be collected using a vacutainer with a blood set collection-wing needle or 20 ml syringe according to the required blood volume. The blood would be put into a blood culture bottle (BACTEC[®]) which is aerobic first then anaerobic. The sample must be sent to the laboratory for a maximum of 24 h at a temperature of 25°C and if Myco/F-lytic must be in a dark-colored paper bag.

The types of examinations that are usually performed with cerebrospinal fluid (CSF) sample was Gram stain and culture. If multiple cultures are performed, the volume of CSF must be >5 ml. The site for CSF collection must be aseptic according to applicable protocol. For CSF that will be cultured aerobically (1–5 ml)/fungi (≥2 ml) would be put into a sterile container, while the anaerobic (1–2 ml) was put into BACTEC[®] anaerobic plus/Medium BD[®]. Sterile body fluids are all the body fluids obtained aseptically such as abdominal fluid, amnion, ascites, joints, paracentesis, pericardial, peritoneal, pleural, synovial, continuous peritoneal dialysis (CAPD), and thoracocentesis. The type of examination is the same as CSF but if there

are many types of culture then the volume of CSF that must be sent was >10 ml. The collection, handling, and processing methods were the same as CSF but different in volume such as bacteria \geq 10 ml and fungi \geq 5–10 ml.

Sputum samples that were used were expectorated, induced, bronchoalveolar lavage (BAL)/ bronchial washing/bronchial brushing. Sputum induced can only do fungal and smear examination. The patients must rinse first with water to remove oral flora and food residue. Sputum will be placed into a sterile container with a screw cap. The sample will be sent a maximum of 24 h with a temperature of 4–8°C using a cool box or dry ice.

The specimens used were indwelling catheters and midstream urine

Anaerobic cultures were not performed from pus/swab from superficial wounds. Instead, swab are cultured for aerobic bacteria and fungal. One swab is only for one site collection. Anaerobic culture for abscess is done using 1–2 ml in BACTEC[®] anaerobic plus/medium BD.

Data management and data analysis

The sensitivity of the sample was identified by the dilution method using a vitex-2 machine. The data would be processed using Microsoft Excel to calculate the sensitivity of microorganisms to antimicrobials with the formula: Sensitive/(sensitive + intermediate + resistant)*100 and the results are in percentage form. The data were also processed using SPSS for analytical calculations regarding the age prevalence of Gram-positive bacteria, Gram-negative bacteria, and *Candida* spp. The data were calculated using ANOVA with the results obtained as mean \pm SD, minimum, maximum, and p-value.

Once ethical approval was obtained there was an entry

This ethical approval was valid from October 28, 2020, to October 29, 2021. Ethical review passes number 162/K-LKJ/ETIK/X/2020.

Results

In Table 1, it can be seen that this study obtained 3,675 samples, there were 1,341 (36.48%) isolates and 2,334 (63.51%) negative cultures. There were 746 (55.63%) males and 595 (44.36%) females. The average age of the population is 56 years, with a standard deviation of 65,66. From 1,342 isolates, there were 800 (59.65%) Gramnegative bacteria, 209 (15.58%) Gram-positive bacteria, and 332(24.75%) *Candida* spp. (Table 1).

Table 1: Data demographics of the study population

Variables	N (%)		
Sex			
Male	746 (55.64)		
Female	595 (44.37)		
Age grup in years			
≤14	72 (5.37)		
15–19	36 (2.68)		
20–24	38 (2.83)		
25–29	42 (3.13)		
30–34	25 (1.86)		
35–39	50 (3.73)		
40–44	39 (2.91)		
45–49	88 (6.56)		
50–54	78 (5.82)		
55–59	194 (14.47)		
≥60	679 (50.63)		
Positive culture	(1341)/n total sample = %		
Gram (+) bacteria	209 (15.58)		
Gram (-) bacteria	800 (59.65)		
Candida spp.	332 (24.75)		
MDROs*	(629)/total positif gram (+) dan (-) = %		
CRE	94 (26.48)		
ESBL	228 (74.03)		
MDR-Ab	100 (68.49)		
KPC	169 (76.47)		
MRSA	23 (32.86)		
VRSA	10 (14.29)		
VISA	2 (2.86)		
VRE	3 (9.38)		

The average prevalence of age from Gram-positive bacteria was 53.93 years, with a standard deviation being 20, 18; in Gram-negative bacteria, the average prevalence of age found was 64.73 years with a standard deviation of 21.05; for *Candida* spp., the average prevalence of age found was 60.74 years, with a standard deviation of 18,87. ANOVA analysis shows p < 0.001, indicating a significant difference in the prevalence of age to Gram-negative bacteria, Gram-positive bacteria, and *Candida* spp. (Table 2).

 Table 2: Prevalence of age to Gram-Negative Bacteria,
 Gram-Negative Bacteria, and Candida spp.

Bacteria/Candida spp.	Age						
	Mean ± SD	Minimun	Maximun	p value			
Gram-Positive	53.93 ± 20.18	2	90	<0.001			
Gram-Negative	54.73 ± 21.05	2	101				
Candida spp.	60.74 ± 18.87	3	94				

Based on the Figure 1, the most common microorganism found in ICU was

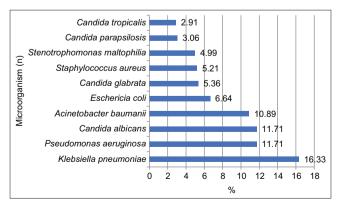


Figure 1: Percentages of ten the most common microorganisms in intensive care unit Siloam Teaching Hospital

Table 3: Distribution of specimen percentage in intensive care unit Siloam Teaching Hospital

Specimen	% (n/1341)	
Sputum	67.48	Achromobacter denitrificans (3), Acinetobacter baumannii (113),
		Acinetobacter junii (3), Acinetobacter ursingii (2), Aeromonas
		hydrophilia (2), Bordetella hinzii (1), Brevundimonas diminuta (2), Budhaldaria appagian (0), Candida alhianna (128), Candida aifarri
		Burkholderia cepacian (9), Candida albicans (138), Candida ciferri
		(2), Candida dubliniensis (2), Candida glabrata (68), Candida
		krusei (8), Candida lipolytica (1), Candida lusitaniae (5), Candida
		mognoliae (1), Candida parapsilosis (31), Candida rugosa (1),
		Candida tropicalis (35), Citrobacter koseri (1), Enterobacter
		aerogenes (3), Enterobacter cloacae (9), Enterococcus faecalis
		(1), Escherichia coli (25), Klebsiella oxytoca (2), Klebsiella
		pneumoniae (171), Kodamaea ohmeri (1), Moraxella group (1),
		Ochrobactrum anthropi (1), Pandoraea species (2), Pantoea spp.
		(1), Proteus mirabilis (2), Providencia rettgeri (1), Providencia
		stuartii (1), Pseudomonas aeruginosa (127), Pseudomonas
		fluorescens (3), Pseudomonas putida (6), Serratia fonticola (1),
		Serratia marcescens (10), Serratia rubidaea (1), Sphingomonas
		paucimobilis (2), Staphylococcus aureus (49), Staphylococcus
		haemolyticus (1), Stenotrophomonas maltophilia (55),
Distri	44.45	Streptococcus pneumoniae (1)
Blood	14.45	Acinetobacter baumannii (13), Acinetobacter junii (1),
		Acinetobacter Iwoffii (1), Burkholderia cepacian (4),
		Burkholderia pseudomallei (1), Candida albicans (2), Candida
		glabrata (1), Candida parapsilosis (6), Candida tropicalis (1),
		Chryseobacterium. Indologenes (1), Citrobacter koseri (1),
		Dermacoccus nishinomiyaensis (1), Enterobacter cloacae
		(1), Enterococcus faecalis (4), Enterococcus. Faecium (2),
		Escherichia coli (17), Gemella morbillorum (1), Klebsiella
		pneumoniae (19), Kocuria kristinae (3), Kocuria varians (1),
		Pseudomonas aeruginosa (7), Pseudomonas fluorescens (1),
		Salmonella spp. (3), Serratia fonticola (1), Serratia rubidaea
		(1), Sphingomonas paucimobilis (3), Staphylococcus aureus
		(13), Staphylococcus auricularis (1), Staphylococcus capitis
		(20), Staphylococcus caprae (2), Staphylococcus cohnii (2),
		Staphylococcus epidermidis (22), Staphylococcus haemolyticus
		(14), Staphylococcus hominis (10), Staphylococcus sciuri 91),
		Stenotrophomonas maltophilia (9), Streptococcus gallolyticus
Urine	8.2	(1), Streptococcus pneumoniae (1)
Unne	0.2	Achromobacter denitrificans (1), Acinetobacter baumannii
		(3), Burkholderia pseudomallei (1), Candida albicans (10),
		Candida krusei (1), Candida parapsilosis (2), Candida
		tropicalis (2), Enterobacter aerogenes (1), Enterobacter cloacae complex (2), Enterococcus faecalis (7), Enterococcus
		faecium (12), Escherichia coli (33), Klebsiella pneumoniae (15), Proteus mirabilis (1), Pseudomonas aeruginosa (6),
		Pseudomonas fluorescens (1), Pseudomonas aeruginosa (0),
		Staphylococcus aureus (1), Staphylococcus epidermidis (2),
		Staphylococcus gallinarum (1), Staphylococcus epidermidis (2), Staphylococcus gallinarum (1), Staphylococcus haemolyticus
		 Staphylococcus vitulinus (1), Streptococcus agalactiae (1), Streptococcus pseudoporcinus (1)
Pus	4.69	Acinetobacter baumannii (6), Candida albicans (1), Candida
1 43	4.05	glabrata (1), Candida tropicalis (1), Enterobacter aerogenes
		(2), Enterobacter cloacae (2), Enterobacter aerogenes
		Enteococcus faecium (4), Escherichia coli (12), Klebsiella
		pneumoniae (6), Pseudomonas aeruginosa (6), Pseudomonas
		aureus (6), Staphylococcus cohnii (1), Staphylococcus
		haemolyticus (5), Stenotrophomonas maltophilia (2),
		Streptococcus anginosus (4)
Bronchial	3.2	Acinetobacter baumannii (9), Burkholderia cepacian (4),
Fluid	0.2	Candida albicans (5), Candida glabrata (1), Candida
		lusitaniae (1), Candida parapsilosis (2), Enterobacter aerogenes
		(1), Enterococcus faecalis (1), Klebsiella pneumoniae (6),
		<i>Mycobacterium tuberculosis (1), Nebsicia preumoniae (0),</i>
		Pseudomonas aeruginosa (8), Pseudomonas fluorescens (1),
		Pseudomonas putida (1), Serratia marcescens (1)
Sterile	1.34	Acinetobacter baumannii (2), Citrobacter freundii (1),
Body	-	Candida albicans (1), Candida glabrata (1), Escherichia
Fluid		coli (1), Klebsiella pneumoniae (2), Pandoraea species (1),
		Pseudomonas aeruginosa (3), Pseudomonas fluorescens
		(1), Pseudomonas putida (1), Staphylococcus capitis (1),
		Staphylococcus epidermidis (2), Stenotrophomonas maltophilia (1)
		Granulicatella elegans (1), Mycobacterium tuberculosis (1),
CSF	0.52	
CSF	0.52	
CSF	0.52	Staphylococcus aureus (1), Staphylococcus epidermidis (2),
CSF Feces	0.52	

Klebsiella spp. 221 (16%), *Pseudomonas spp.* 176 (13%), and *Candida albicans* 157 (12%). Table 3 shows that the most common specimen found in ICU was sputum 905 (67.48%) and blood 194 (14.45%).

Table 4: Antimicrobials resistance pattern of predominant microorganisms isolated from patients admitted in intensive care unit of siloam teaching hospital (%)

Antimicrobial	<i>Escherichia</i> <i>coli</i> (n = 89)	Pseudomonas. (n = 176)	<i>Klebsi ella</i> spp. (n = 221)	Sternotropho monas maltophilia (n = 66)	<i>Acinetobacter</i> spp. (n = 153)	<i>Staphylococcus</i> <i>aureus</i> (n = 70)	<i>Enteroco</i> <i>ccus</i> spp. (n = 32)	<i>GP-CONS</i> (n = 91)	<i>Candida</i> spp. (n = 332)
Amoxicillin	12	-	0	-	-	12	55	12	
Amoxicillin/clavulanic acid						67	53	21	
Ampicillin	12	0	0	3	1	9	53	4	
Ampicillin/sulbactam	39	19	24	94	39	69	50	22	
Piperacillin/tazobactam	81	37	34	59	20				
Cefoperazone/sulbactam	100	72	55	72	82				
Cefotaxime	34	0	25	10	50	67	0	19	
Cefepime	74	51	39	-	20	67	75	20	
Ceftazidime	46	40	27	47	17	66	0	21	
Ceftriaxone	34	1	26	8	7	63	0	19	
Cefoperazone	35	49	22	44	12	67	0	30	
Doripenem						67	0	21	
Ertapenem	100	0	49	-	1				
Imipenem	99	48	82	10	28	68	56	25	
Meropenem	100	44	52	11	28	70	80	29	
Gentamycin	73	47	55	39	22	88	0	43	
Amikacin	100	62	62	42	54				
Levofloxacin	32	51	34	64	26	84	24	29	
Moxifloxacin						83	0	29	
Fosfomycin	88	36	64	33	27				
Tigecycline	100	2	51	58	80	97	100	99	
Doxycycline						94	100	91	
Azithromycin						81	-	23	
Linezolid						94	74	80	
Teicoplanin						93	90	93	
Tetracycline						56	16	70	
Trimethoprim/sulfamethoxazole	51	13	50	84	46				
Amphotericin B	-	-		-	-				88
Fluconazole									75
Voriconazole									97
Micafungin									96

Table 4 shows that the antibiotic with the highest sensitivity to Gram-negative bacteria was cefoperazone/sulbactam 74%, amikacin 62%, and imipenem 59%. However, antibiotic with the lowest sensitivity of antibiotic for Gram-negative bacteria was cefazolin 2%, ampicillin 3%, and amoxicillin 4%. The antibiotic with the highest sensitivity for Gram-positive bacteria was tigecycline 98%, doxycycline 95%, and teicoplanin 91%. The antibiotic with the lowest sensitivity for Gram-positive bacteria was cefadroxil 20%, benzylpenicillin 25%, and amoxicillin 27%. Table 3 shows that the antifungal with the highest sensitivity for *Candida* spp. was amphotericin B 88%, fluconazole 75%, flucytosine 90%, micafungin 96%, and voriconazole 97%.

Discussion

The study found the average age was 56 years because older adults mostly have comorbidities such as diabetes mellitus and arthritis and they have an immune system that is no longer function well. The combination makes older adults more susceptible to infection. The most prevalent bacteria were Gram-negative bacteria. There were significant results between the age and prevalence of Gram-negative bacteria, Gram-positive bacteria, and *Candida* spp. Patients at high risk for candida infection in the ICU were the patients who have prior surgery, acute renal failure, whose nutrition is given parenterally, and patients who use a central venous catheter. We know that patients who are in the ICU are patients who often use a catheter, so they are susceptible to candida infection. The average age of patients infected with candidiasis in the ICU was 60.3 years [9].

From this study, we learned that the most common microorganism in ICU was Klebsiella spp. Klebsiella spp., Pseudomonas aeruginosa, Escherichia coli, and Staphylococcus aureus were microorganisms that are often found in ICU patients in Asian countries, especially Indonesia [10]. Klebsiella pneumoniae is a bacterium that colonizes the oropharynx and gastrointestinal tract which often causes bacteremia, ventilator-associated pneumonia, septicemia, surgical site infections, and urinary tract infections and also plays an important role in opportunistic infections that occur in immunocompromised patients [11]. A study in India showed that the most common microorganisms found in ICU patients were Acinetobacter baumannii (20,9%), K. pneumoniae (19,7%), E. coli (18,3%), and P. aeruginosa (14,0%) [12]. Research conducted in India showed that there were 53.9% of hospital-acquired pneumonia cases and 8,95 per 1,000 ventilator-acquired pneumonia cases. A study conducted in Pakistan showed hospitalacquired pneumonia cases were about 55% and a study conducted in China showed about 41.2% of ventilatoracquired pneumonia cases [13].

Sputum was the most common specimen in ICU Siloam Teaching Hospital. Infectious diseases that occur in ICU patients are hospital-acquired pneumonia and ventilator-acquired pneumonia, so in diagnosing pneumonia, it is necessary to take the patient's sputum to know the pattern of antimicrobial sensitivity that is used in treatment [13]. A study in Dhaka showed that microorganisms were most found in sputum and tracheal aspirates because most patients had respiratory problems and were on ventilators [14].

This study showed that Gram-positive bacteria had the highest sensitivity to tigecycline and doxycycline. However, studies done in Aurangabad, Bali, and Manado showed that the antibiotics with the highest sensitivity to Gram-positive bacteria were linezolid and vancomycin [3], [8], [15]. Meanwhile, the antibiotics with the highest sensitivity for Gram-negative bacteria were cefoperazone/sulbactam and amikacin. In Aurangabad. the antibiotics with the highest sensitivity for Gramnegative bacteria were amikacin and imipenem. In Bali, the antibiotics with the highest sensitivity for Gram-negative bacteria were cefoperazone/sulbactam, piperacillin/ tazobactam, meropenem, and cefepime [3], [8]. Based on research conducted at the Aurangabad ICU, it showed that the most microorganisms were S. aureus (51%) and antibiotics that were most sensitive to E.coli were imipenem (79%), amikacin (79%), ampicillin (32%) [8]. A study was conducted in Dr. Soetomo Hospital Surabava found more Gram-negative bacteria than Gram-positive bacteria. Gram-negative bacteria were found in specimens of blood (66.01%) and sputum (66.67%). P. aeruginosa had highest sensitivity to the antibiotics cefosulbactam (88,09%), amikacin (78,57%), ampicillin (0%), and amoxicillin/clavulanate (0%) [16].

The highest sensitivity of antifungals for *Candida* spp. was voriconazole and micafungin. The highest sensitivity of antifungals for *Candida* spp. in China was amphotericin and fluconazole, but in Venezuela and India, they were voriconazole and fluconazole [17], [18], [19]. From the results, antimicrobial sensitivity from each study had a different sensitivity pattern, where it could be influenced by the way antimicrobials which are used by clinicians in the area. The use of antimicrobials greatly affects the occurrence of resistance in some microorganisms. Where in developing countries, one of which is Indonesia, it was found that 84% of patients were given antimicrobials, whereas about 32% of these patients were given antimicrobials without appropriate indications [9].

Research done in Pekan Baru showed that rational antimicrobial use in the ICU is 67.7% and there were about 8.82% of clinicians who give antimicrobial without indications. Clinical behavior that is not by the protocol of antimicrobial administration in the hospital also does not monitor antibiotic therapy properly so it can cause some types of antimicrobial to become resistant [2]. This study had some limitations in that all the data were taken from a database of microbiology laboratory, so the researchers were not able to analyze risk factors and comorbidities of any data that could affect the results of the sensitivity to antimicrobial. In addition, there was still some incomplete data so it can affect the calculation of sensitivity. However, the advantage in this study was the huge number of samples included over a long period so that it can represent the pattern of microorganisms and their sense of the ICU Siloam Teaching Hospital.

Conclusions

This study showed that the sensitivity of antimicrobials was no longer effective in treating infection. Therefore, the government and doctors must play an important role in socializing the correct way of using antimicrobial. Controlling the use of antimicrobials can reduce the cost and length of treatment for patients with infectious diseases.

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