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PREVALENCE AND CHARACTERISTICS OF MULTIDRUG-RESISTANT *ACINETOBACTER BAUMANNII* CASES AT THE DR. WAHIDIN SUDIROHUSODO GENERAL HOSPITAL IN MAKASSAR

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ABSTRACT

Multidrug-resistant *Acinetobacter baumannii* (MDRAB) is a strain that is resistant to three or more classes of antibiotics. As the prevalence of MDRAB increases, the antibiotics of choice become limited. Identification of MDRAB is required to manage and control infection.This research was conducted to determine the prevalence and characteristics of MDRAB in the Wahidin Sudirohusodo Hospital Makassar. This research was a retrospective study, conducted from January to December 2016. Bacterial identification and antimicrobial susceptibility testing (AST) were performed using VITEK 2. The patient data were obtained from the medical records. A total of 323 *Acinetobacter baumannii* isolates was obtained, consisting of 188 isolates in January-June 2016 and 36 of which were MDRAB (19.15%) with the average length-of-stay 33 days; and 135 isolates in July-December 2016 and 31 of which were MDRAB (22.96%) with the average length-of-stay 27 days. Multidrug-resistant *Acinetobacter baumannii* was mostly discovered from patients using three or more medical devices and on a single antibiotic therapy. Multidrug-resistant *Acinetobacter baumannii* isolates were mostly obtained from sputum and pus specimens, and the majority of patients had an infection and respiratory diseases. The most comorbid diseases in MDRAB were endocrine-metabolic diseases. The result of AST showed 100% and 96% susceptibility to Polymyxin B; 71.43% and 54.84% to Amikacin; 66.67% and 50% to Trimethoprim/Sulfamethoxazole, respectively. Prevalence of MDRAB in 2016 increased from January-June (19.15%) to July-December (22.96%), suggesting a need to identify patients at risk for MDRAB infection and to promote the rational use of antibiotics. Polymyxin B, Amikacin, and Trimethoprim/Sulfamethoxazoleare the antibiotics of choice to treat MDRAB.

Key words: *Acinetobacter baumannii*, multidrug-resistant *Acinetobacter baumannii*, antibiotic resistance

INTRODUCTION

Acinetobacter is a group of bacteria often found in soil and water. Acinetobacter has many species which can all cause disease in humans, and 80% of Acinetobacter infections are reported to be caused by *Acinetobacter baumannii*.[1,2] *Acinetobacter baumannii* is a Gram-negative coccobacillus that is aerobic and pleomorphic. This organism is also hydrophilic and forms colonies in aqueous environments. Besides, genes Acinetobacter is often considered as the cause of hospital and medical device-acquired infections, especially in developing countries. *Acinetobacter baumannii* is also known to be responsible for 2–10% of Gram-negative bacterial infections in hospitals. *Acinetobacter baumannii*, more over, is often found in sputum or respiratory secretions, wounds, and urine in hospitalized patients. Some factors that tend to increase the risk of Acinetobacter infection are irrational exposure to antibiotics, intensive care unit care, use of central venous catheters, use of mechanical ventilation, and hemodialysis that do not meet medical service standards.[3-8] *Acinetobacter baumannii*, furthermore, can last a long time in a variety of environmental conditions. This organism is also known to be responsible for causing various infections, namely pneumonia, bacteremia, meningitis, urinary tract infections, and wound infections. On the other hand, it is resistant to many types of antimicrobials, so treatment options for patients infected with this bacterium become limited. Thus, infection due to Multidrug-resistant *Acinetobacter baumannii* (MDRAB) is associated with a high mortality rate, around 26-68% of severely ill ICU patients.[4,6,8]

Multidrug-resistant *Acinetobacter baumannii* is a strain of *Acinetobacter baumannii* that is resistant to three classes of antibiotics or more. The incidence of in-vitro resistance of Acinetobacter baumannii isolates has increased since the 1970s. Previously, this group of bacteria was still sensitive to the often used antimicrobials. In 2007, the incidence of

MDRAB reached 70%, depending on the country, hospital, medical department, and clinical sample. Besides, this group of bacteria is also known to be resistant to Carbapenem. Carbapenem is a drug used to treat MDRAB cases. Research conducted by Hasan *et al*. in 2013 in hospitals in Pakistan found that there were 59 of 90 *Acinetobacter baumannii* isolates resistant to Carbapenem, and 87 isolates were multidrug-resistant.[3,4,8,9]

Similarly, a research at the ICU Sanglah Hospital in Denpasar found that *Acinetobacter baumannii* isolates were resistant not only to the Carbapenem group, namely Imipenem with a sensitivity of 28%, but also to other antibiotics, such as Trimethoprim/ Sulfamethoxazole with a sensitivity of 25%, and Amikacin with a sensitivity of 36%. Besides, a research conducted by Dewi *et al*. at the Arifin Achmad Hospital in Riau Province from January 1 to December 31, 2014, also found that 45.9% of 246 *Acinetobacter baumannii* isolates were resistant to Meropenem.[10,11]

Therefore, MDRAB identification is very necessary for the management of antibiotic therapy and infection control. Unfortunately, the number of researches on MDRAB in Indonesia is still small and has never done in Makassar. Hence, this research was conducted to determine the prevalence and characteristics of MDRAB cases in two periods, namely January-June 2016 and July-December 2016 at the Dr.Wahidin Sudirohusodo General Hospital, Makassar.

METHODS

This research was a retrospective descriptive study. Data used in this research were obtained from the Clinical Pathology Laboratory of the Tropical Infectious Disease Sub-Unit and Medical Record Installation of the Dr. Wahidin Sudirohusodo General Hospital in Makassar. Research samples were secondary documents reporting results of antibiotic sensitivity tests on *Acinetobacter baumannii* isolates from January-December 2016, which isolation and identification used VITEK 2 and which fulfilled inclusion criteria, namely complete medical record data.

Subsequently, secondary data obtained from the Clinical Pathology Laboratory of Tropical Infectious Disease Sub-Unit consisted of patients' identity, types of specimen, treatment rooms, and results of antibiotic sensitivity tests. The other data then were collected from medical records in the forms of diagnosis, length of treatment, history of antibiotic administration, and use of medical devices, such as infusion, urine catheter, ventilator, Central Venous Catheter (CVC), and Hemodialysis (HD). Afterward, the data were analyzed using descriptive statistics, which results were displayed in tables.

RESULTS AND DISCUSSION

From January to December 2016, there were 323 data of *Acinetobacter baumannii* isolates divided into two-time period groups, namely January-June 2016 with a total of 188 isolates and July-December 2016 with a total of 135 isolates. After antibiotic sensitivity tests were conducted on those isolates, there were 36 MDRAB isolates (19.15%) for the period January-June 2016, and increased in the period July-December 2016 were 31 MDRAB isolates (22.96%).

Next, the characteristics of the multidrug-resistant *Acinetobacter baumannii* isolates were evaluated as illustrated in Table 1.

Multidrug-resistant *Acinetobacter baumannii* isolates in the January-June 2016 period in this research were obtained in the same number for males and females. Besides, the data revealed that MDRAB isolates in the January-June 2016 period were mostly found in the age groups of ≤ 18 years and>60 years. Multidrug-resistant *Acinetobacter baumannii* isolates in the January-June 2016 period were also known to be mostly found at the use of ≥ 3 medical devices (50%). This research also found that the most MDRAB incidence in the January-June 2016 period was found in the use of one type of antibiotic equal to 41.67%. The average length of treatment for those patients with MDRAB in this period was 33 days.

Furthermore, in the period of July-December 2016 in this research, the highest number of MDRAB isolates was found in females. This research also showed that MDRAB isolates in the period of July-December 2016 were primarily found in the age group of ≤ 18 years. Like in the January-June 2016 period, MDRAB isolates in the July-December 2016 period were also known to be mostly found in the group with the use of ≥ 3 medical devices (45.16%). Based on the number of antibiotics used, this research then showed that the incidence of MDRAB was mostly found in the use of one type of antibiotics (41.94%). The average length of treatment for patients with MDRAB was 27 days.

Most MDRAB cases in the period of January-June 2016 were found in sputum specimens (30.55%), whereas in the period July-December 2016 MDRAB cases were mostly found in pus specimens (41.94%). Based on the diagnosis, MDRAB was primarily form in patients with a diagnosis of infectious disease

Table 1. Characteristics of MDRAB samples

Variables	January - June 2016 (n = 36)	July - December 2016 (n = 31)
Sex		
Male	18 (50%)	14 (45.16%)
Female	18 (50%)	17 (54.84%)
Age		
≤ 18	11 (30.56%)	10 (32.26%)
19 – 40	4 (11.11%)	8 (25.81%)
41 – 60	10 (27.77%)	9 (29.03%)
> 60	11 (30.56%)	4 (12.90%)
Use of medical devices (infusion devices, catheter, CVC, HD, ventilator)		
0 – 1	11 (30.56%)	11 (35.48%)
2	7 (19.44%)	6 (19.36%)
≥ 3	18 (50%)	14 (45.16%)
Use of antibiotics in the hospital		
1 types of antibiotics	15 (41.67%)	13 (41.94%)
2 types of antibiotics	13 (36.11%)	11 (35.48%)
3 types of antibiotics	8 (22.22%)	5 (16.13%)
4 types of antibiotic	-	2 (6.45%)
Average length of treatment (minimum-maximum) (days)	33 (5-145)	27 (6-93)

Source: The secondary data

(19.44%) in the period January-June 2016, whereas in the period July-December 2016 it was mostly diagnosed in respiratory system disease (22.58%). In this research, endocrine-metabolic diseases, diabetes mellitus with kidney disease complication, especially chronic kidney failure were considered as comorbid diseases mostly found in MDRAB patients in the period January-June 2016, whereas in the period July-December 2016 lung disease, especially pulmonary TB or pneumonia were the most comorbid diseases in MDRAB patients (see Table 2).

Based on the data from treatment room records, the highest prevalence of MDRAB was found in internal medicine care unit rooms both in the period January-June 2016 and in the period July-December 2016 (see Table 3).

The results of the MDRAB sensitivity tests for antibiotics in the period January-June 2016 showed that they were 100% sensitive to Polymyxin B, 71.43% sensitive to Amikacin, and 66.67% sensitive to Trimethoprim/Sulfamethoxazole. The highest resistance (100%) was also found in several antibiotics, namely Ampicillin, Amoxicillin-Clavulanic acid, Aztreonam, Cefazolin, Nitrofurantoin, and Cefoxitin (see Table 4).

The results of the MDRAB sensitivity test for antibiotics in the July-December 2016 period were 96% sensitive to Polymyxin B, 54.84% sensitive to Amikacin, 50% sensitive to Trimethoprim/Sulfamethoxazole. The highest resistance (100%) was also found in several antibiotics, namely Ampicillin, Amoxicillin-Clavulanic acid, Aztreonam, Tetracycline, Cefazolin, Nitrofurantoin, and Cefoxitin (see Table 4).

Moreover, the results of this research revealed that the prevalence of MDRAB at the Dr. Wahidin Sudirohusodo General Hospital in Makassar from January to June 2016 increased from 19.15% to 22.96% in the period of July-December 2016. The use of medical devices was also known to be a risk factor for *Acinetobacter baumannii* infection since MDRAB was mostly found in the use of ≥ 3 medical devices. Similarly, some previous researches also found that the use of medical devices became a risk factor for *Acinetobacter baumannii* infection.[3,12]

Furthermore, this research also showed that MDRAB was mostly found in the use of one type of antibiotics. Like this research, some previous studies also found that the use of one type of antibiotics usually used a broad spectrum was considered as a risk factor for Acinetobacter baumannii infection.[3,12]

Acinetobacter baumannii is often found in sputum

Table 2. Characteristics of MDRAB isolates based on specimen types and diagnosis

Variables	January-June 2016 MDRAB (n = 36)	July-December 2016 MDRAB (n = 31)
Specimen types		
Urine	4 (11.11%)	1 (3.23%)
Sputum	11 (30.55%)	9 (29.03%)
Bronchial rinse	2 (5.56%)	-
Pus	9 (25%)	13 (41.94%)
Blood	4 (11.11%)	2 (6.45%)
Stool	2 (5.56%)	-
Endotracheal tube	4 (11.11%)	6 (19.35%)
Diagnosis		
Infectious disease respiratory system	7 (19.44%)	6 (19.35%)
disease	6 (16.67%)	7 (22.58%)
Urogenital system disease	3 (8.33%)	1 (3.23%)
Cardiovascular system disease	2 (5.56%)	2 (6.45%)
Gastrointestinal system diseases	4 (11.11%)	3 (9.68%)
Nervous system disease	3 (8.33%)	4 (12.90%)
Musculoskeletal system disease	-	3 (9.68%)
Immunological system disease	1 (2.77%)	-
Hematological system disease	-	1 (3.23%)
Endocrine and metabolic disease	2 (5.56%)	-
Skin and subcutaneous tissue disease	4 (11.11%)	3 (9.68%)
Neoplasma	4 (11.11%)	-
ENT disease	-	1 (3.23%)
Comorbid disease		
Lung disease	2 (5.56%)	6 (19.35%)
Endocrine-metabolic disease	6 (16.67%)	4 (12.90%)
Cardiovascular disease	2 (5.56%)	4 (12.90%)
Kidney disease	6 (16.67%)	3 (9.68%)
Malignancy	2 (5.56%)	1 (3.23%)

Source: The secondary data

Table 3. MDRAB prevalence based on treatment rooms

Treatment rooms	January-June 2016 (n = 36)	July-December 2016 (n = 31)
Childcare room	4 (11.11%)	-
Internal medicine treatment room	13 (36.11%)	11 (35.49%)
Surgical treatment room	3 (8.33%)	6 (19.35%)
Burn treatment room	3 (8.33%)	2 (6.45%)
Skincare room	1 (2.78%)	-
ENT treatment room	-	1 (3.23%)
ICU	7 (19.45%)	3 (9.68%)
PICU	5 (13.89%)	4 (12.90%)
NICU	-	4 (12.90%)

Source: The secondary data

or secretion, respiratory, wound, and urine of hospitalized patients. Previous research even argued that MDRAB was mostly found in sputum and pus specimens. Meanwhile, *Acinetobacter baumannii* infection was mostly found in the respiratory tract.[3] Similarly, MDRAB in this research was mostly found in patients with infectious diseases and respiratory system diseases. The most comorbid conditions found in this research were endocrine-metabolic disease, kidney disease, and lung disease.

Finally, the results of this research revealed that MDRAB was 100% sensitive to Polymyxin B in the period of January-June 2016, but the sensitivity decreased to 96% in the period of July-December

Table 4. The results of the susceptibility test of multidrug-resistant Acinetobacter baumannii towards antibiotics

Antibiotics	January-June 2016 (n = 36)			July-December 2016 (n = 31)		
	S	I	R	S	I	R
	n (%)	n(%)	n(%)	n (%)	n(%)	n(%)
Group of Penicillin						
Ampicillin	0	0	34 (100)	0	0	28 (100)
Amoksisilin-Clavulanic Acid	0	0	14 (100)	0	0	25 (100)
Ampicillin-Sulbactam	12 (52.17)	6 (26.09)	5 (21.74)	4 (66.66)	1 (16.67)	1 (16.67)
Piperacillin-Tazobactam	7 (20.59)	0	27 (79.41)	5 (17.86)	1 (3.57)	22 (78.57)
Group of Cephalosporin						
Cefazolin	0	0	20 (100)	0	0	3 (100)
Cefoxitin	0	0	14 (100)	0	0	25 (100)
Cefotaxime	1 (7.14)	0	13 (92.86)	1 (3.57)	2 (7.14)	25 (89.29)
Ceftazidime	7 (19.44)	0	29 (80.56)	4 (12.90)	1 (3.23)	26 (83.87)
Ceftriaxone	3 (8.82)	4 (11.77%)	27 (79.41)	0	6 (19.35)	25 (80.65)
Cefepime	6 (30)	0	14 (70)	3 (100)	0	0
Cefoperazone-Sulbactam	2 (15.38)	4 (30.77%)	7 (53.85)	10 (40)	4 (16)	11 (44)
Group of Carbapenem						
Doripenem	1 (7.14)	0	13 (92.86)	6 (24)	0	19 (76)
Imipenem	1 (7.14)	0	13 (92.86)	6 (24)	0	19 (76)
Meropenem	10 (27.78)	0	26 (72.22)	10 (32.26)	1 (3.23)	20 (64.51)
Group of Monobactam						
Aztreonam	0	0	21 (100)	0	0	3 (100)
Group of Aminoglycoside						
Amikacin	25 (71.43)	3 (8.57)	7 (20)	17 (54.84)	5 (16.13%)	9 (29.03)
Gentamycin	9 (26.47)	1 (2.94)	24 (70.59)	7 (22.58)	0	24 (77.42)
Tobramycin	1 (7.14)	3 (21.43)	10 (71.43)	6 (24)	7 (28%)	12 (48)
Group of Tetracycline						
Doxyxycline	5 (31.25)	0	11 (68.75)	14 (50)	0	14 (50)
Tetracycline	1 (50)	0	1 (50)	0	0	3 (100)
Group of Sulfonamide						
Trimetoprim-Sulfametaxazole	14 (66.67)	0	7 (33.33)	3 (50)	0	3 (50)
Group of Fluoroquinolone						
Ciprofloxacin	7 (31.82)	0	15 (68.18)	3 (50)	0	3 (50)
Levofloxacin	1 (6.67)	3 (20)	11 (73.33)	3 (10.71)	3 (10.71%)	22 (78.58)
Norfloxacin	0	0	1 (100)			
Group of Glycylcyclines						
Tigecycline	13 (65)	7 (35)	0	3 (100)	0	0
Group of Polypeptide						
Polymyxin B	14 (100)	0	0	24 (96)	0	1 (4)
Group of other antibiotics						
Chloramphenicol	0	0	1 (100)			
Nitrofurantoin	0	0	20 (100)	0	0	3 (100)

Source: The secondary data

2016. Like this research, some previous investigations also found that Polymyxin B was currently been considered as an appropriate antibiotic to treat MDRAB infections because of its high level of sensitivity. However, there were still some strains of Acinetobacter baumannii resistant to Polymyxin B.[13-15]

CONCLUSION AND SUGGESTIONS

The prevalence of MDRAB in the Dr. Wahidin Sudirohusodo General Hospital in 2016 was high. Hence, all relevant parties should be concerned with risk factors for MDRAB, including the use of medical

Table 5. *Acinetobacter spp.*; anti-microbial categories and agents used to define MDR, XDR, and PDR (worksheet for categorizing isolates).[16]

Antimicrobial category	Antimicrobial agent	Results of antimicrobial susceptibility testing (S or NS)
Aminoglycosides	Gentamicin Tobramycin Amikacin Netilmicin	
Antipseudomonal carbapenems	Imipenem Meropenem Doripenem	
Antipseudomonal fluoroquinolones	Ciprofloxacin Levofloxacin	
Antipseudomonal penicillins + β-lactamase inhibitors	Piperacillin-tazobactam Ticarcillin-clavulanic acid	
Extended-spectrum cephalosporins	Cefotaxime Ceftriaxone Ceftazidime Cefepime	
Folate pathway inhibitors	Trimetoprim-sulphamethoxazole	
Penicillins + β-lactamase inhibitor	Ampicillin-sulbactam	
Polymyxins	Colistin Polymyxin B	
Tetracyclines	Tetracycline Doxycycline Minocycline	

Criteria for defining MDR, XDR, and PDR in *Acinetobacter spp.*
MDR: non-susceptible to ≥1 agent in ≥3 antimicrobial categories
XDR: non-susceptible to ≥1 agent in all but ≤2 categories
PDR: non-susceptible to all antimicrobial agents listed

devices. Based on the results of this research, Polymyxin B., Amikacin, and Trimethoprim/ Sulfamethoxazole were known to be appropriate antibiotics still sensitive to MDRAB.

As a result, to prevent and control MDRAB infections, identification of risk for MDRAB infection in patients must be conducted first, such as whether patients use many medical devices and whether they are medically treated for a long time. Also, rational antibiotic therapy should also be provided, improved, and monitored as recommended by the Standard of Procedure (SOP) for nosocomial infection.

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