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The prevalence of carbapenem-resistant *Acinetobacter baumannii* in Ulin General Hospital Banjarmasin

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Abstract
Acinetobacter baumannii has the most bacteria found and had resistance toward several antibiotics. this study finding out the prevalence of Carbapenem-resistant *Acinetobacter baumannii* (CRAB) and the antibiotic sensitivity pattern toward *A. baumannii* isolated in Ulin General Hospital Banjarmasin. This study aimed to identify the prevalence of CRAB (Carbapenem-resistant *Acinetobacter baumannii*) and some antibiotics sensitivity pattern toward *A. baumannii*. The study was a cross-sectional study conducted by using a retrospective descriptive methodology. The population of this study was all of the patients suspected with infection that subjected to a culture testing in the Infection Division Department of Clinical Pathology Laboratory of Ulin General Hospital in Banjarmasin between January 1 and December 31, 2016. The obtained data was then analyzed descriptively. The sample was collected using total sampling and it was performed at Infection Division Department of Clinical Pathology Laboratory of Ulin General Hospital in Banjarmasin. Data was descriptively presented by using the frequency distribution table for taking the conclusion. *Acinetobacter baumannii* has the most bacteria found and had resistance toward several antibiotics. The result showed total isolate of A. baumanii was 70/2836, prevalence 70/1239. CRAB isolate was 43/70 (61%). The prevalence of *Acinetobacter baumannii* was 5.65%, while the prevalence of CRAB was 3.47%. Antibiotic application in the hospital should be the basis of empirical antibiotic administration by clinicians. Prevention efforts of bacterial infection transmission need to be elevated to minimize the bacteria resistance toward antibiotic inpatient.

Keywords: *Acinetobacter baumannii*, antibiotic, infection

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INTRODUCTION

Antibiotic is the most administered drug related to bacterial infection. It has function as the prophylaxis to prevent and restrain major infections for high-risk patients. Therefore, rational antibiotic administration will be an essential thing to be considered. Rational antibiotic administration for the last five decades has dramatically increased. The Center for Disease Control and Prevention in the USA stated that there were about 50 million unnecessary prescribing out of 150 million prescribing by year. Several studies in Indonesia found 40-62% of inappropriately administered for diseases in which not needed.

This inappropriate antibiotic administration might generate major problem as the developing of antibiotic-resistant bacteria or antibiotic resistance occurrence. It has been a global problem either in developed or developing countries (Fauziyah et al. 2011). The antibiotic resistance continuously occurred and widely spread out and thus this world will be back to the pre-antibiotic era (Aminov 2010).

Bacteria resistant prevalence is linear to the number of antibiotics administered. This has been proved by the antibiotic-resistant increased which found in the hospital. Patients are potential to have an antibiotic resistance as their immunity decreased, suffered from the comorbid disease, and inevitably contacted to invasive equipment. The diseases frequently occurred such as sepsis and nosocomial infection might also have an impact on bacteria resistance (Brun-Buisson et al. 2004, Zahar et al. 2014).

Empirical therapy rapidly reduces the morbidity and mortality rate of highly infected patients by considering pathogen suspected to cause infection, bacterial resistant pattern, and risk factors of patients including resistant risk.

Acinetobacter baumannii is an opportunistic pathogen frequently leading to either severe or nosocomial infection that particularly for

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immunocompromised patients who were hospitalized for a long time (Sieniawski et al. 2013). *Acinetobacter baumannii* is a Gram-negative bacillus that is aerobic, pleomorphic, and non-motile. *A. baumannii* has a high incidence among immunocompromised individuals, particularly patients who have experienced a prolonged (>90 d) hospital stay. It has been shown to colonize on the skin. Moreover, it is also highly isolated from the respiratory and oropharynx of infected individuals (Fauziyah et al. 2011). Therefore, it has been designated as a "red alert" human pathogen in recent years. This is also generating alarm among the health professionals which largely arising from an extensive antibiotic resistance spectrum (Sieniawski et al. 2013).

The phenomenon of multidrug-resistant (MDR) pathogens has increasingly become a serious concern to both nosocomial and community-acquired infections. Indeed, the World Health Organization (WHO) has recently identified antimicrobial resistance as one of the three most important problems of human health (Zahar et al. 2014). The most common and serious MDR pathogens have been encompassed within the acronym "ESKAPE," which stands for *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* sp (Brun-Buisson et al. 2004). While in the 1970s *A. baumannii* is thought to have been sensitive to most antibiotics, today the pathogen appears to exhibit extensive resistance to most first-line antibiotics.

According to the Centers for Disease Control and Prevention (CDC) report, A. baumanii resistance toward carbapenem increased from 9% in 1995 into 40% in 2004 (Brun-Buisson et al. 2004). According to Sieniawski et al. 2013 during his study in Asia and the Middle East, it found that the most infections were caused by multi-drug resistant *A. baumannii* toward some antibiotic groups.

Carbapenem resistance is a major public health problem globally. It occurs mainly among Gram-negative pathogens such as *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*. It can be intrinsic or mediated by transferable carbapenemase-encoding genes. This type of resistance genes is widespread in certain parts of the world, particularly Europe, Asia, and South America. In brief, the situation in Indonesia, especially Banjarmasin is not appropriately documented. In this paper, we provide prevalence of carbapenem resistance *Acinetobacter baumanii* providing up-to-date information on the subject (Sieniawski 2013).

The study in Indonesia exhibited that Acinetobacter is one of the most important opportunistic Gram-negative bacteria with a prevalence of 25.8% and usually found in weakened patient (Zahar et al. 2014). Carbapenem (specifically imipenem and meropenem) is the major antimicrobial used to treat infectious patients by Acinetobacter. However, this treatment might lead to bacteria resistance toward carbapenem. The study conducted in ICU of Sanglah General Hospital Denpasar stated that *Acinetobacter baumannii* (29%) was the most bacteria easily found. This bacterium had been reported as being resistant to the carbapenem group, including imipenem with 28% sensitivity, then another antibiotic such as trimethoprim /sulfamethoxazole with 25% sensitivity, and amikacin with 36% sensitivity.

Data from bacteria culture and antibiotic sensitivity test are becoming the strategies to control the antibiotic administration and antibiotic-resistant prevention. Of these data, the one in Ulin General Hospital for the last several years, *A. baumannii* has also ranked in ten for the most bacteria found and had resistance toward several antibiotics. Based on those factors, this study aimed to identify the prevalence of CRAB (Carbapenem-resistant *Acinetobacter baumannii*) and some antibiotics sensitivity pattern toward *A. baumannii* isolated in Ulin General Hospital Banjarmasin between January 1 and December 31, 2016.

MATERAL AND METHODS

Type and Design of the Research

The study was a cross-sectional study conducted by using a retrospective descriptive methodology. In this study, we conducted an observational study and analyze the data from a studied population.

Population and Sample

The population of this study was all of the patients suspected with infection that subjected to a culture testing in the Infection Division Department of Clinical Pathology Laboratory of Ulin General Hospital in Banjarmasin between January 1 and December 31, 2016.

Collection of Information

The sample was collected using total sampling and it was performed at Infection Division Department of Clinical Pathology Laboratory of Ulin General Hospital in Banjarmasin. Data was obtained from *A. baumannii* positive culture result and antibiotic resistance test within blood, urine, pus, sputum, and other liquid bodies of patients hospitalized on Ulin General Hospital in Banjarmasin between January 1 and December 31, 2016.

The other data collected based on the variables taken from Vitek 2 compact. It was the tool for culture test and antibiotic resistance in accordance with the number of data written on register book between January 1 and December 31, 2016. Patient specimens were taken from various patient rooms at Ulin Banjarmasin Hospital. Positive culture results from patients suspected of infection were taken from the medical record of the patient's ward and the type of specimen. The ward was divided into adult inpatients

(*Anggrek*, *Anggrek 2nd*, *Dahlia*, Class 1, Class 3, PDW), VIP inpatient room (Aster, Utama B), Surgery room, Outpatient polyclinic (Diabetes Outpatient Polyclinic, Clinical Laboratory, Lung Outpatient Clinic), and Intensive Care Unit (ICU, NICU, HCU-Teratai).

Data and statistical analysis

Data was descriptively presented by using the frequency distribution table for taking the conclusion. Percentage (%) of the antibiogram sensitivity obtained from the amount of sensitivity to the certain antibiotics divided by the total number of isolates of *Acinetobacter baumannii* in one year.

Bioethical aspect

We didn't need any ethical clearance as we only take the secondary data from the hospital's laboratory as the main data in this study.

RESULT

A. baumannii Isolates Results

The study was analyzing 2836 samples culture from patients and it showed that 1239 (44%) samples are showing positive results. Furthermore, it also demonstrated that 70 isolates obtained from the blood specimen, urine, pus, sputum, and other body liquid of patients had *A. baumannii* growth. *A. baumannii* growth was found within 22 isolates (31%) from blood specimen, 8 isolates (12%) from urine specimen, 15 isolates (21%) from pus specimen, 19 isolates (27%) from sputum specimen, and 6 isolates (9%) from other liquid specimens (Fig. 1). The data of *A. baumannii* isolated from blood, urine, pus, sputum specimen, and other body liquid is presented in Table 1.

Based on the origin of care room, *Acinetobacter baumannii* specimen is mostly obtained from 29 isolates (41.4%) of intensive unit: ICU, NICU and Teratai ward (HCU) and the third-class ward was the second largest, 23 isolates (32,9%). Data are presented in Table 2 and Fig. 2.

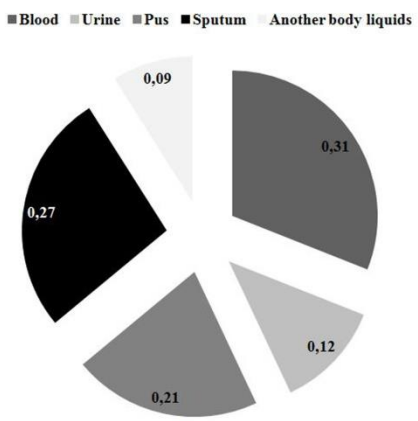

Fig. 1. Specimen origin distribution from *A. baumannii* isolation of patients hospitalized in Ulin General Hospital, Banjarmasin.

Table 1. The data of *A. baumannii* isolated from blood, urine, pus, sputum specimen, and other body liquid

No	Specimen type	Number of isolates	(%)
1	Blood	22	31
2	Urine	8	12
3	Pus	15	21
4	Sputum	19	27
5	Other body liquid	6	9
	Total	**70**	**100**

Table 2. *A. baumannii* distribution in the culture of all specimens collected from the wards in Ulin General Hospital, Banjarmasin

No	Ward	Isolate number	(%)
1	*Anggrek*	1	1.4%
2	*Anggrek 2nd floor*	1	1.4%
3	*Aster*	1	1.4%
4	Surgery	1	1.4%
5	*Dahlia*	1	1.4%
6	Diabetic feet	1	1.4%
7	First class	5	7.14%
8	Third class	23	32.9%
9	Clinical Lab	1	1.4%
10	Lung	3	4.3%
11	PDW	2	2.9%
12	Primary B	1	4.3%
13	Intensive Care (ICU, NICU, HCU Teratai)	29	41.4%
	Total	70	

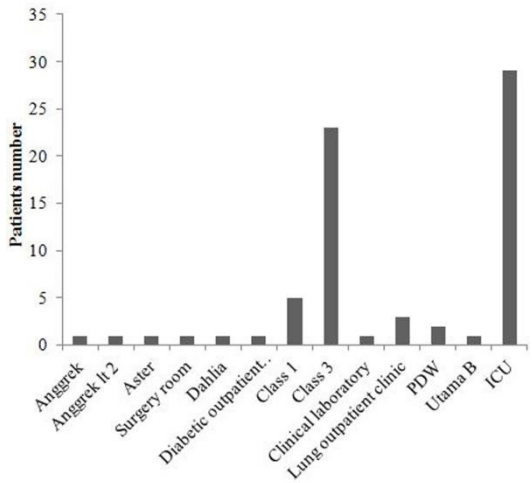

Figure 2. *A. baumannii* distribution in a culture of all patient specimens collected from wards in Ulin General Hospital, Banjarmasin.

A. baumannii Resistance Patterns

A. baumannii resistance pattern based on the initial patient ward in Ulin General Hospital, Banjarmasin is presented in Table 2.

A. baumannii Sensitivity Pattern

Antibiotic sensitivity pattern toward *A. baumannii* from patients hospitalized in Ulin General Hospital, Banjarmasin presented in Table 3. The result showed that the tigecyclin was the susceptible antibiotics with good sensitivity (64 isolates with 94% efficacy). As an alternative, trimethropin/sulfametohxazol was the next susceptible one, with 53% isolates (76%) were sensitive to this antibiotics.

Table 3. Antibiotic sensitivity pattern distribution toward *A. baumannii* from patients hospitalized in Ulin general hospital Banjarmasin

No	Antibiotics	Isolate number (n)	% Efficacy
1	Amikacin	55	79
2	Gentamicin	29	41
3	Ceftazidime	22	31
4	Ceftriaxon	3	4
5	Cefepime	23	33
6	Meropenem	43	61
7	Ampicillin/sulbactam	48	69
8	Ciprofloxacin	25	36
9	Piperacillin/Tazobactam	28	40
10	Trimethoprim/sulfamethoxazole	53	76
11	Tigecycline	64	91

Color description:

: Sensitivity 0% — 49%

: Sensitivity 50% — 75%

: Sensitivity 76% — 100%

DOSCUSSION

Based on the report obtained from Infection Division of Clinical Pathology Laboratory of Ulin General Hospital, Banjarmasin between 2015 and 2016, there was an increasing number of *A. baumannii* infection found from 2.71% into 5.65%. Further study in clinical and laboratory basis on CRAB resistance incidence are needed for assessing some etiology risk factors with the more complete medical record.

It can be suggested that guidelines are needed to assist the rational use of antibiotics based on their hospital data. Antibiotic application in the hospital should be the basis of empirical antibiotic administration by clinicians. Prevention efforts of bacterial infection transmission need to be elevated to minimize the bacteria resistance toward antibiotic inpatient. The bacteria pattern and antibiotic resistance in Ulin General Hospital, Banjarmasin in every year need to be addressed for further analysis.

The high incidence of Gram-negative bacteria in hospitals is being the reason for administration of antibiotic grouped aminoglycoside as empirical therapy. Related to this study, amikacin is one of the chosen antibiotics for the management of infectious etiology in Ulin General Hospital, Banjarmasin. Trimethoprim/sulfamethoxazole and tigecycline antibiotic combination can be another choice for administration. This combination comes from different classes. In addition, to provide a synergistic effect, it also has a function to prevent the resistance incidence. This is essential as the initial antibiotic therapy related to the increased mortality rate. Therefore, it can be stated that one strategy to optimize the antibiotic application and antibiotic resistance is by applying the combination. *A. baumannii* is mostly sensitive to amikacin, trimethoprim/sulfamethoxazole, and tigecycline.

In 2011, Microbiology Laboratory of ICU in Cipto Mangunkusumo Hospital reported that there was an increasing number of *A. baumannii* infection found from 11% into 23.3%. Moreover, the study in ICU of Sanglah Central Public Hospital, Denpasar from July to December 2013 found that the bacteria culture result was mostly Gram-negative: *A. baumannii* (28.9%), P. aeruginosa (16.3%), and K. pneumoniae (7.4%) followed by Gram-positive bacteria: CoNS (6%) (Zahar et al. 2014). Similarly, the study performed by Sheth et al. in ICU India discovered that bacteria causing sepsis in ICU was *A. baumannii* (6.1%) (Sheth et al. 2012). *Acinetobacter baumannii* is one of aerobic Gram-negative bacteria widely spread on the ground and water, then skin, mucous membrane, and secrete in human. These bacteria can survive on some surfaces (either wet or dry) in the hospital environment

(Manchanda et al. 2012). This organism naturally resistance to several antibiotics and colonizes within the patients in the hospital. The systemic invasion has caused pneumonia, septicemia, meningitis or urinary tract infection. The infection commonly occurs in patients with excessive antibiotics and application of medical equipment including a cannula or intubation. Nosocomial infection is one of the cases obtained during hospitalization. It occurred after 48 hours of admission. Most patients do not feel any symptom and do not belong to the incubation period at the first admission (Rotstein et al. 2008).

Based on the study by Silma in Dr. Kariadi Central Public Hospital, Semarang, the patients in intensive care unit had 5.6 times chance (95%CI= 1.307-23.996) to be infected by CRAB as compared to patients who did not get to intensive care. The study in South Korea exhibited that patients within intensive care had the experience to be infected by carbapenem-resistant Acinetobacter sp. as 21.5 times higher than those without getting into intensive care (Lee et al. 2004). Acinetobacter infection is frequently occurred to the patients with treatment in ICU and invasive medical equipment including central venous infusion, mechanical ventilation, catheter, and others (Brun-Buisson et al. 2004). Underlying diseases, long hospitalization period, wide range spectrum of antibiotic administration, and resistant microorganism colonization are several risk factors for nosocomial infection (Aminov 2010, Sieniawski et al. 2013).

Acinetobacter can survive for quite a long time on the inanimate surface, for instance, medical equipment, patient bed, cupboard, table, pillow, and linen. Long exposure to the hospital environment, poor infection control, and lack prevention effort induce the higher potential of Acinetobacter colonization and resistant toward various groups of antibiotics as well as increasing cross-transmission (Brun-Bussion et al. 2004, Sieniawski et al. 2013). Acinetobacter transmission sources in the hospital commonly come from medical officers' hands and the inanimate surface area (Brun-Bussion et al. 2004).

Based on the result of a bacteria resistance test, it demonstrated that *A. baumannii* had been resistant toward antibiotics grouped carbapenem with efficacy 61%. Whilst another group of β-lactamase such as ceftazidime, ceftriaxone, cefepime is having efficacy about 41%, 4%, and 31%, respectively. Moreover, the fluoroquinolone (ciprofloxacin) group has efficacy about 36%, and other antibiotic groups such as piperacillin/Tazobactam has 40%. The antibiotic sensitivity that remained in good condition and showed good efficacy is Amikacin 79%, Trimethoprim/sulfamethoxazole 76%, and Tygecycline 91%.

This study is in accordance with other study in ICU of Sanglah Central Public Hospital, Denpasar which demonstrated that *A. baumannii* had been resistant to carbapenem group, including imipenem with 28% of sensitivity, likewise to other antibiotics such as trimethoprim/sulfamethoxazole with 25% of sensitivity, and amikacin with 36% of sensitivity. In a study conducted in Sanglah Central Public Hospital, Denpasar between July and December 2014, it was found that *A. baumannii* sensitivity level was 39% with certain resistance level toward carbapenem groups such as imipenem about 50 of 217 bacteria and meropenem about 37 of 217 bacteria. The similar thing also demonstrated by Jamshidi et al. in Iran which stated that Acinetobacter sp. had been resistant to the therapy of antibiotic such as imipenem by having sensitivity 47.7% and another antibiotic such as cefepime by having sensitivity 0% (Jamshidi et al. 2009).

However, the different study reported by Sheth et al. 2012 in ICU India, stated that *A. baumannii* had 100% sensitivity with meropenem). *A. baumannii* is generally effective to some antibiotic groups such as beta-lactam and aminoglycoside (Jamshidi et al. 2009). This is because the pattern of bacteria in each place or each hospital is different. The administration of broad-spectrum antibiotics and their combinations is the management of infectious diseases by clinicians. This is one of the supporting factors to change the pattern of infectious bacteria and patterns of resistance to various antibiotics. During its development, *A. baumannii* might be resistant to various antibiotics due to support by particular clinic condition such as patient. As described earlier, in this study, *A. baumannii* had been resistant to beta-lactam group such as carbapenem. However, it still has sensitivity toward aminoglycoside group including amikacin by having 79% sensitivity, tigecycline by having 91% sensitivity, and trimethoprim/sulfamethoxazole by having 76% sensitivity.

The study performed by Sheth et al. 2012 in an ICU in India discovered that *A. baumannii* had 100% sensitivity toward amikacin. It is relatively different from Widyatmoko's study in ICU of Dr. Kariadi Central Public Hospital, Semarang. It found that *A. baumannii* had been resistant toward tigecycline and cotrimoxazole with sensitivity 45% and 39%, respectively. Then, the study resulted by Jamshidi et al. 2012 in Iran revealed that *A. baumannii* also had low sensitivity toward amikacin about 31.8% (Jamshidi 2009). Based on the our study concluded that the most bacteria and had resistance toward several antibiotics was *Acinetobacter baumannii* with total was 70/2836 isolates and prevalence was 5.65%. Whereas, CRAB isolate was 43/70 isolates in total with prevalence was 3.47%.

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REFERENCES

Aminov RI (2010) A brief history of the antibiotic era: Lessons learned and challenges for the future. Frontiers in Microbiology 1:1-7. https://doi.org/10.3389/fmicb.2010.00134

Brun-Buisson C, Meshaka P, Pinton P, Vallet B (2004) EPISEPSIS: A reappraisal of the epidemiology and outcome of severe sepsis in French intensive care units. Intensive Care Med 30:580-8. https://doi.org/10.1007/s00134-003-2121-4

Fauziyah S, Radji M, Aribinuko N (2011) The relationship of the use of antibiotics in empirical therapy with bacterial sensitivity in ICU Fatmawati General Hospital Jakarta. Indonesian Pharmacist Journal 5:150-8. https://doi.org/10.35617/jfi.v5i3.50

Jamshidi M, Javadpour S, Eftekhari TE, Moradi N, Jomehpour F (2009) Antimicrobial resistance pattern among intensive care unit patients. African Journal of Microbiology Research 3:590-4. https://doi.org/10.5897/AJMR.9000086

Lee SO, Kim NJ, Choi SH, Kim TH, Chung JW, Woo JH, Ryu J, Kim YS (2004) Risk factors for acquisition of imipenem-resistant *Acinetobacter baumannii*: A case control study. Antimicrobial Agents and Chemotherapy 48:224-8. https://doi.org/10.1128/aac.48.1.224-228.2004

Manchanda V, Sanchaita S, Singh NP (2012) Multidrug resistant Acinetobacter. Journal of Global Infectious Diseases 2:291-304. https://doi.org/10.4103/0974-777X.68538

Rotstein C, Evans G, Born A, Grossman R, Light RB, Magder S, McTaggart B, Weiss K, Zhanel GG (2008) Clinical practice guidelines for HAP and VAP in adults. The Canadian Journal of Infectious Diseases and Medical Microbiology 19:19-53. https://doi.org/10.1155/2008/593289

Sheth KV, Patel TK, Malek SS, Tripathi CB (2012) Antibiotic sensitivity pattern of bacterial isolates from the ICU of a tertiary care hospital in India. Tropical Journal of Pharmaceutical Research 11(6): 991-999. https://doi.org/10.4314/tjpr.v11i6.17

Sieniawski K, Kaczka K, Gaqis L, Pomorski L (2013) *Acinetobacter baumannii* nosocomial infections. Polski Przeglad Chirurgiczny 85:483-90. https://doi.org/10.2478/pjs-2013-0075

Zahar JR, Lucet JC, Timsit JF (2014) Antimicrobial resistance in intensive care units The Lancet. Infectious diseases 14:3-5. https://doi.org/10.1016/S1473-3099(13)70305-0