

Brief Original Article

Association of *Acinetobacter Baumannii* with invasive procedures in hospitalized patients in Jakarta

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Abstract

Introduction: *Acinetobacter baumannii*, a multidrug-resistant Gram-negative opportunist has been known among the cause of nosocomial infection. Risk factors of infection related to *A. baumannii* have been reported elsewhere. This study aimed to find the association of *A. baumannii* positive culture and invasive procedures in patients hospitalized in the Intensive Care Unit and Hospital ward in Jakarta.

Methodology: This study was a retrospective, 1:1 matched case-control study with total sampling method from in-patients in the ICU and the Internal Medicine Wards (IMW) of a Private Hospital, North Jakarta in 2015 - 2018. Data retrieved were positive culture of *A. baumannii*. Positive cultures of multi-sensitive bacteria were included as a control group. Antibiotic susceptibility test was carried out as recommended by Clinical and Laboratory Standards Institute.

Results: A total of 88 in-patients were studied, and *A. baumannii* isolates were identified from 44 patients. Most of *A. baumannii* showed resistant to almost all antibiotics tested, except for colistin. Bivariate analysis showed a significant association of *A. baumannii* positive culture and the use of ventilator in the ICU ($p = 0,039$), and with urinary catheters in the IMW ($p = 0,022$). Multivariate analysis showed that length of stay also has a significant association to *A. baumannii* positive culture in the ICU.

Conclusions: The use of ventilators and urinary catheters showed a significant association with *Acinetobacter baumannii* positive culture in patients in the ICU and in the IMW respectively. All of the *A. baumannii* isolates were susceptible to colistin.

Key words: *Acinetobacter baumannii*; nosocomial infection; invasive procedures.

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Introduction

Acinetobacter baumannii (*A. baumannii*) is a Gram negative bacillus opportunistic pathogen, and well known as among the most pathogen that cause Hospital Acquired Infection (HAI) [1]. During the last decade, there is an increase in numbers of nosocomial infection caused by *A. baumannii* [2], and the rapid spread of the infections are of a great concern nowadays. Also, since this pathogen is a multidrug-resistant in which the infection may lead to a lack of effective therapeutics, long hospital stay, and high rates of mortality [3]. Prevalence of *A. baumannii* infection was high in many places from Asia, Africa, Europe and United State of America, the percentage varies between as low as 5.6% in Western Europe to 19.2% in Asia [4]. In Indonesia, the report from Haji Adam Malik Hospital in Medan showed 17,44% (644/3693) infections caused by *A. baumannii* [5]. A study in the Neonatal unit in the Public Hospital, Jakarta showed 18.9% *A. baumannii* positive culture from a total of 37 blood cultures from neonates with sepsis [6]. Similar condition was also

found in one of Private Hospital in North Jakarta; out of a total of 92 identified isolates from all kinds of specimens received in our laboratory in 2016, 14.1% were *A. baumannii* [7]. Earlier studies showed the use of invasive devices among other ventilator, central venous catheter, urinary catheter, enteral tube feeding, intravenous catheter, arterial catheter, nasogastric tube in patients are among the risk factors of *A. baumannii* infection. *A. baumannii* can form biofilm in the abiotic surface so that it can grow well on the surface of devices used by patients and cause infection. Hospitalized patients with many invasive procedures, even more with lower immune status, they are prone to infection; long duration of hospital stay and use of antibiotics add more risks of *A. baumannii* infection and the resistance [8–10]. This study aimed to determine the association of positive *A. baumannii* culture and the use of invasive devices from patients hospitalized in the Intensive Care Unit and the Internal Medicine Wards in the Private Hospital in North Jakarta.

Methodology

Study design

This was a retrospective, 1:1 matched case-control study with whole sampling method. Medical records from patients hospitalized in the Intensive Care Unit (ICU) and in the Internal Medicine Wards (IMW) of the Private Hospital Atma Jaya, in North Jakarta during January 2015-December 2018 were examined. Patients with positive culture of *A. baumannii* were included in the case group, while those with positive culture of multi-sensitive drugs bacteria were the control group. Invasive devices used by the patients were noted.

Risk factor analysis

The following data were collected: gender, age, length of hospitalization stay, treatment with antimicrobial agents, admission diagnosis, and usage of invasive procedures (ventilator, central venous catheter, urinary catheter, enteral tube feeding, intravenous catheter, arterial catheter). This study focused on the use of invasive devices and their association with *A. baumannii* positive culture.

Statistical analysis

Data analysis was performed using SPSS software version 23. For risk factor analysis, chi-square test was used. P values of <0.05 considered significant.

Antibiotic susceptibility test

Antimicrobial susceptibility test (AST) was conducted as recommended by Clinical and Laboratory Standards Institute (CLSI) [11]. and carried out using disc diffusion method. All records of antibiotic susceptibility of *A. baumannii* were retrieved from WHONET; antibiotic susceptibility of 80% or greater was determined as good activity in-vitro.

Ethical Clearance

This study has passed ethical evaluations by the Faculty of Medicine and Health Sciences of Atma Jaya Catholic University of Indonesia, No. 05/05/KEP-FKUAJ/2019 and No. 17/12/KEP-FKUAJ/2018.

Results

The present study involved a total of 88 patients, in which 34 patients from the ICU and 54 patients from the IMW. *A. baumannii* positive cultures were found from 17 ICU patients, in which 10 were male (58.8%) and 7 were female (41.2%); from the control group i.e. those of which multi-sensitive drugs bacteria were isolated, number of male patients were also higher (Table 1). Mean of the age was 43 years old in the case group and 48.7 years old in the control group (Table 1). In the IMW, the case group consisted of 27 patients, the number of male patients was also higher than the female ones; though in the control group the female patients

Table 1. Demographic Characteristics and Admission Diagnosis of Patients in Atma Jaya Hospital Jakarta, and Type of Specimens collected.

Parameters	<i>Acinetobacter baumannii</i>		Multidrug sensitive bacteria	
	ICU ^a N (%)	IMW ^b N (%)	ICU ^a N (%)	IMW ^b N (%)
Demographic Characteristic				
Gender				
Men	10 (58.8)	15 (55.6)	9 (53)	13 (48)
Women	7 (41.2)	12 (44.4)	8 (47)	14 (52)
Age (Mean)	43	50	48.7	55
Admission Diagnosis				
Cardiovascular disease	3 (17.6)	3(11.1)	5 (29.4)	5 (18.5)
Respiratory disease	7 (41.1)	12 (44.4)	3 (17.6)	12 (44.4)
Neurologic disease	1 (5.8)	1 (3.7)	2 (11.7)	1 (3.7)
Surgical	3 (17.6)	0 (0)	1 (5.8)	0 (0)
Urogenital disease	1 (5.8)	1 (3.7)	0(0)	3 (11.1)
Endocrine disease	0 (0)	2 (7.5)	2 (11.7)	2 (7.5)
Infection	2 (11.7)	0 (0)	4 (23.5)	0 (0)
Sepsis	0 (0)	8 (29.6)	0 (0)	3 (11.1)
GIT disease ^c	0 (0)	0 (0)	0 (0)	1 (3.7)
Type of Specimens				
Pus	0 (0)	5 (18.5)	2 (11.8)	5 (18.5)
Sputum	13 (76.4)	14 (51.9)	8 (47.1)	17 (63.0)
Blood	2 (11.8)	0 (0)	6 (35.3)	4 (14.8)
Throat swab	0 (0)	0 (0)	1 (5.8)	0 (0)
Urine	2 (11.8)	8 (29.6)	0 (0)	1 (3.7)

^a: Intensive Care Unit; ^b: Internal Medicine Ward; ^c: Gastrointestinal Tract Disease.

were dominant (Table 1). The mean age was 50 years old for patients with *A. baumannii* positive culture, and 55 years old for those with multidrug-sensitive bacteria positive culture (Table 1).

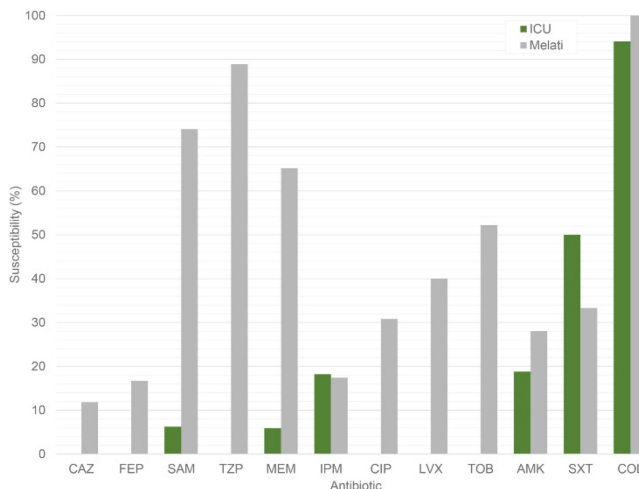
Most of the patients in the ICU (7/41.1%) admitted to the hospital due to respiratory diseases. At the same time, those in the IWM, the number of cases contracted respiratory infection were also the highest, i.e., 12/44.4% (in the case group) and 12/44.4% (in the control group) (Table 1). Amongst various specimens collected, sputum was the highest from both the ICU and IMW patients (Table 1).

Table 2 showed that 94.2% patients in the ICU with *A. baumannii* positive culture were hospitalized >7 days, and only 1 patient (5.8%) in less than 7 days. While in the Internal Medicine Ward, more patients contracted with *A. baumannii* i.e. 59.3% were hospitalized >7 days (Table 2). In the control group, patients with multidrug-sensitive bacteria, the number of patients contracted with these microorganisms were higher in patients with length of stay in hospital >7 days.

A. baumannii isolates originated from patients in ICU were extensively drug-resistant (14/17, 82.4%); of 17 isolates resistance was as follow: to ampicillin-sulbactam (93.8%), piperacillin-tazobactam (100%), ceftazidime (100%), cefepime (100%), meropenem (94.1%), imipenem (81.8%), ciprofloxacin (100%), levofloxacin (100%), gentamicin (90.9%), and amikacin (81.2%). Meanwhile, those originated from patients in the IMW, 13 out of 27 *A. baumannii* isolates (48.1%) were extensively drug-resistant; nonetheless good activity was shown against piperacillin-tazobactam (88.9%). Is important to note that *A. baumannii* isolates from both ICU and IMW patients showed high susceptibility to colistin, i.e. 94.1% and 100% respectively (Figure 1).

Table 3 showed that a higher number of patients in the ICU with *A. baumannii* 12 (66.7%) used a ventilator than those infected by multidrug sensitive bacteria, which was half less. The urinary catheter was the second-highest device used in the ICU. In the IMW, those with urinary catheters contracted more the *A. baumannii* than the multidrug sensitive bacteria. Bivariate analysis of risk factors of *A. baumannii* positive culture and invasive procedures revealed a significant association between the use of mechanical ventilators and *A. baumannii* in patients in the ICU ($p = 0.039$) (Table 3). Furthermore, there was also a significant association between the use of urinary catheters and *A. baumannii* in patients in the IMW ($p = 0.022$) (Table 3). The use of other invasive devices in

Figure 1. Susceptibility patterns of *A. baumannii* isolates from patients in the Intensive Care Unit and the Internal Medicine Ward in Atma Jaya Hospital from 2015 to 2018.



ICU: Intensive care Unit, IMW: Internal Medicine Ward. Almost all *A. baumannii* isolates from both ICU and IMW showed high resistant to antibiotics tested, but colistin showed good activity (>80%). In addition, isolates from IMW also showed good activity to piperacillin-tazobactam.

Antibiotics tested were as follow: CAZ: Ceftazidime, FEP: Cefepime SAM: Sulbactam-ampicillin, TZP: Piperacillin-tazobactam, MEM: Meropenem, IPM: Imipenem, CIP: Ciprofloxacin, LVX: Levofloxacin, TOB: Tobramycin, AMK: Amikacin, SXT: Sulphamethoxazole, COL: Colistin.

the ICU patients, i.e. central venous catheter (CVC), urinary catheter, and enteral tube feeding (ETF), however, was not significantly related to *A. baumannii* positive culture. Further, intravenous (IV) catheter was applied to all patients, hence statistical analysis cannot be performed; no one was found using the arterial catheter. In the IMW, the use of IV catheter and nasogastric tube was found to be insignificant in relation to *A. baumannii* positive culture.

Length of stay of hospitalization, divided into 2 categories as follow: < 7days and >7 days, was also examined. Multivariate analysis using logistic regression showed that two independent risk factors in the ICU were identified: ventilator usage (Odds ratio (OR) 5.633, 95% Confidence Interval (CI) 1.069-29.680, p 0.041) and length of hospitalization stay (OR 0.072, 95% CI 0.007-0.761, p 0.029) (Table 4). Although this study focused on the use of invasive devices, we found out that length of stay was also has a significant association with *A. baumannii* positive culture in ICU inpatients. In the IMW, multivariate analysis showed only urinary catheter usage (OR 0.11, 95% CI 0.012-0.967, p 0.047) showed a significant association with *A. baumannii* positive culture (Table 5).

Table 2. Duration of Hospitalisation of patients in the ICU and IMW.

Parameters	<i>Acinetobacter baumannii</i>		Multidrug sensitive bacteria	
	ICU ^a N (%)	IMW ^b N (%)	ICU ^a N (%)	IMW ^b N (%)
≤ 7 days	1 (5.8)	11 (40.7)	7 (41.2)	12 (44.4)
> 7 days	16 (94.2)	16 (59.3)	10 (58.8)	15 (55.6)

^a: Intensive Care Unit; ^b: Internal Medicine Ward.

Table 3. Bivariate Analysis of Invasive Procedures Related to *A. baumannii* Positive Culture.

Procedure	<i>Acinetobacter baumannii</i>		Multidrug sensitive bacteria		p value (ICU ^a)	p value (IMW ^b)
	ICU ^a N (%)	IMW ^b N (%)	ICU ^a N (%)	IMW ^b N (%)		
Ventilator	12 (66.7)	NA ^e	6 (33.3)	NA ^e	0.039	NA ^e
CVC ^c	3 (17.6)	NA ^e	2 (11.7)	NA ^e	0.628	NA ^e
Urinary Catheter	10 (58.8)	7 (25.9)	10 (58.8)	1 (3.7)	1.00	0.022
ETF ^d	9 (52.9)	4 (14.8)	10 (58.8)	1 (3.7)	0.730	0.159
IV Catheter ^f	17 (100)	27 (100)	17 (100)	27 (100)	0.a	0.a

^a: Intensive Care Unit; ^b: Internal Medicine Ward; ^c: Central Venous Catheter; ^d: Enteral Tube Feeding; ^e: Not Analysed; ^f: Intravenous Catheter.

Table 4. Multivariate Analysis of Risk Factor for *A. baumannii* Positive Culture in The ICU.

	Odds Ratio	95% CI	p value
Ventilator usage	5.633	1.069-29.680	0.041
Length of hospitalisation	0.072	0.007-0.761	0.029
Urinary catheter	0.321	0.032-3.222	0.344
Enteral tube feeding	0.664	0.111-3.957	0.653
Central Venous Catheter	1.108	0.109-11304	0.931

Table 5. Multivariate Analysis of Risk Factor for *A. baumannii* Positive Culture in The IMW.

	Odds Ratio	95% CI	p value
Urinary catheter	0.11	0.012-0.967	0.047
Nasogastric tube	0.305	0.028-3.286	0.327
Length of hospitalisation	1.744	0.521-5.841	0.367

Discussion

This study showed that there was a significant association between ventilator usage and *A. baumannii* positive culture in patients hospitalized in the ICU ($p = 0.039$). *A. baumannii* can form biofilm on the surface of the intubation tube which directly entered the respiratory tract. The bacteria can survive on the surface until months so that it will always be the source of infection if disinfection is not carried out properly [12]. Therefore, the incidence of *A. baumannii* infection in patients with ventilator is increasing significantly. Moreover, patients in the ICU mostly immunocompromised, so they are more prone to an infection or colonization. Uwingabiye *et al.*, 2017 [9] showed that there was a significant association between the use of ventilator and *A. baumannii* colonization by multivariate analysis; it increased 6.9 times risk of acquiring *A. baumannii* positive culture. Consistent with other studies, Baran *et al.* [13], 2007 showed a significant relationship between the use of endotracheal tube and imipenem resistant *A. baumannii* (IRAB) ($p = 0,031$); among all patients with *A. baumannii* culture positive, 53.7% patients infected with IRAB. Moreover, invasive procedure and the duration of usage have been shown as one of the risk factors of *A. baumannii* infection [13, 14]. Multivariate analysis by Graciagarmendia *et al.*, 2001 [15] also reported that mechanical ventilator has a significant association with *A. baumannii* infections.

In the present study, the use of CVC in ICU patients showed insignificant results. The same condition was also reported by a study which conducted in the University Hospital in Spain with 42 ICU patients with *A. baumannii* bacteremia [15]. Further, the use of nasogastric tube and *A. baumannii* positive culture in both ICU and IMW patients showed no significance. On the contrary Wong *et al.*, 2002 [16] showed a significant association between nasogastric tube and *A. baumannii* infection in which the subjects of the investigation were patients in the Burns unit. Burn patients particularly prone to infection because of loss of their protective skin and mucosal barrier and reduced in immunity, therefore *A. baumannii* can easily enter the body and infect the patients.

In this study, the association between urinary catheter and *A. baumannii* infection in ICU patients was not significant, while there was a significance between urinary catheter and *A. baumannii* positive culture in patients in the IMW ($p = 0.022$). Using univariate analysis, Zhou *et al.*, 2018 [17] at the First Affiliated Hospital, School of Medicine, Zhejiang University, showed 91.2% patients with *A. baumannii* bacteremia

were due to urinary catheter. So did the study by Garcia-Garmendia *et al.*, 2001 which showed a significant association between urinary catheter and *A. baumannii* infection [15].

Acinetobacter baumannii isolates in the present showed extensively resistant to almost all antibiotics tested except to colistin, although some isolates from the IMW were still susceptible to ampicillin-sulbactam and piperacillin-tazobactam; this condition was quite similar to those isolated in the National Hospital, Cipto Mangunkusumo Hospital in Jakarta [6].

Conclusions

This study showed a significant association between the use of ventilator and urinary catheter with *A. baumannii* positive culture in patients hospitalized in the ICU and hospital ward respectively. Other invasive devices, however, were not associated with the presence of *A. baumannii*. In addition, length of stay was also found to be associated with *A. baumannii* positive culture in patients in hospitalized in ICU. *A. baumannii* isolates from ICU and hospital ward were susceptible to colistin. This information obtained is worth noted that the use of invasive devices can be the source of pathogenic bacteria colonization and infection such as *A. baumannii*, and so good practice must be employed accordingly.

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