Risk Factors for Multi-Drug Resistant Acinetobacter Baumannii Nosocomial Infection

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Objective: *To assess factors associated with multi-drug resistant Acinetobacter baumannii (MDR-AB) nosocomial infection.*
Material and Method: *This hospital-based case-control study was conducted in patients admitted to Siriraj Hospital, Bangkok, Thailand between January 1, 2005 and December 31, 2005. The study population consisted of 155 cases with MDR-AB nosocomial infection and 310 controls without nosocomial infection. The cases were matched with controls by age and ward of admission with a ratio of 1:2.*
Results: *The average age of the present study population was 63.5 $\pm$ 18.7 years among cases and 62.9 $\pm$ 18.2 years among controls. The mean of length of stay in hospital among cases was 4.9 $\pm$ 1.4 weeks and controls 1.8 $\pm$ 1.0 weeks. The most common site of MDR-AB nosocomial infection was lower respiratory tract (74.8%). The antimicrobial susceptibility of MDR-AB was 3.9% to cetriaxone and 42.1% to cefoperazone/sulbactam. Multiple logistic regression analysis showed the following associated factors with MDR-AB nosocomial infection: duration of admission prior to MDR-AB nosocomial infection > 1 week (OR = 2.06; 95%CI 1.09-3.89), indwelling urinary catheter > 1 week (OR = 8.24; 95%CI 3.81-17.82), mechanical ventilation >1 week (OR = 5.73; 95%CI 2.96-11.10), central venous line > 1 week (OR = 3.29; 95%CI 1.48-7.31), nasogastric intubation > 1 week (OR = 6.22; 95%CI 3.24-11.93), prior administration of 3rd-4th generation cephalosporins (OR = 1.80; 95%CI 1.04-3.13), metrodazole (OR = 2.59; 95%CI 1.21-5.56), and piperacillin-tazobactam (OR = 4.68; 95%CI 1.93-11.32).*
Conclusion: *A case-control study in medical and surgical patients in Siriraj Hospital in 2005 revealed risk factors for AB nosocomial infection. Prolonged admission of more than 2 weeks, use of devices, and prior treatment with certain antimicrobials were found to be significant risk factors for the infection. To reduce the infection, strict infection control measures must be applied to the patients with these risk factors. Education to medical personnel and enforcement of infection control practices are all needed to reduce antimicrobial resistant bacterial nosocomial infection.*

Keywords: *Risk factors, Multidrug-resistant, Acinetobacter baumannii, Nosocomial Infection*

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Acinetobacter baumannii (AB) has emerged as a significant nosocomial pathogen in hospitalized patients worldwide. *Acinetobacter baumannii* is a non-fermenting, gram-negative coccobacillus, which lives in soil and water, survives for a long period on dry surfaces, and can probably be transmitted via dust and fomites. Most clinical isolates represent colonization rather than infection, but serious and sometimes fatal infections occur in compromised patients, including

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septicemia, endocarditis, meningitis, and pneumonia[1,2]. The ability of AB to acquire multiple resistances, as well as to survive on skin and in the environment, undoubtedly contributes to its success as a nosocomial pathogen[3]. *Acinetobacter baumannii* can cause pneumonia, tracheobronchitis, bloodstream, urinary tract, and cathether-related and wound infections. Although the infections caused by AB are typically "low-grade", due to the severely ill nature of the patient affected, crude mortality is high, typically ranging from 20-60% and attributable mortality is approximately 10-20%[4]. Reports from various locations around the world, AB comprised 1.3% of nosocomial bloodstream infections in the US SCOPE project between 1995 and 2002. In the SENTRY surveillance between 1997 and 1999, the prevalence of *Acinetobacter* spp. among nosocomial bacteremias ranged from 0.7% in Canada and to 4.3% in Latin America and in Spain, the rate was up to 9.6%[5]. *Acinetobacter* spp. were responsible for 6.9% of pneumonia, 2.4% of bloodstream infections, 2.1% of surgical site infections and 1.6% of urinary tract infections in intensive care units across USA in 2003[6]. Equally concerning was the increase in reports of MDR-AB bacteremia from 7% to 22% in UK in 2003 compared to 2002[7]. In the USA, the proportion of *Acinetobacter* pneumonia in ICU increased from 4% in 1986 to 7% in 2003[8]. In the meantime, carbapenem resistance by MDR-AB was also increasing in the USA, with the rate of resistance increasing from 1.8% in 1996 to 7.3% in 2002 and a further 6.2% showing intermediate resistance by 2002[9]. In Thailand, data from the National Antimicrobial Resistance Surveillance Center (NARST) showed that in vitro activities of common antibiotics against AB decreased during 1998 and 2003. The susceptibility rate of imipenem decreased from 98% to 65%, ceftazidime from 40% to 33%, amikacin from 48% to 38% and ciprofloxacin from 45% to 34%[10,11]. The point prevalence survey in 42 hospitals across Thailand showed that AB ranked third among all Gram-negative pathogens, the average cost of antimicrobials for the treatment of an episode of nosocomial infection was 5,919 baht, and the mortality rate in patients with nosocomial infection was as high as 13.8%. Nosocomial infection was the direct cause of death in 6.7% of patients and was a contributory cause in 3.0%[12]. In the USA, the average cost of treatment for burn patients who acquired MDR-AB was $98,575[13].

The purpose of the present study was to identify risk factors for MDR-AB nosocomial infection. The results from the present study might be valuable for building strategies to prevent MDR-AB nosocomial infection, which is a major health problem in both developed and developing countries, especially for Siriraj Hospital in Bangkok, Thailand.

Material and Method

A hospital-based case-control study was conducted among patients aged over 15 years, admitted between January 1, 2005 and December 31, 2005 in Siriraj Hospital. Cases were patients who had the first episode of MDR-AB nosocomial infection, and were resistant to more than two classes of antimicrobial agents[14]. Cases from medical and surgical departments were identified from records of Infection Control Center, Siriraj Hospital; two controls who did not have nosocomial infection for each case, were randomly chosen from patients who stayed in the same department and were of the same age. One hundred and fifty five cases and 310 controls were included in the analysis. Data were mainly retrieved from hospital records of patients and from the Infection Control Center in Siriraj Hospital. Variables explored were age, gender, co-morbidity (diabetes, malignancy, cerebrovascular accidents, pulmonary and renal diseases), severity of illness by APACHE II score, length of stay in hospital, surgery, chemotherapy, radiotherapy, immunosuppressive drug, urinary catheterization, mechanical ventilation, central venous lines, nasogastic intubation, and antimicrobial drugs. Univariate analysis was used to identify significant risk factors and 95% confidence interval followed by multivariate logistic regression to assess risk factors for MDR-AB. A p-value of less than 0.05 was considered statistically significant.

Results

1. Characteristics of study population

The cases from the medical department were about two-thirds of all. The number of cases in general wards and intensive care units of the two departments were almost equal. The age of the cases and controls were 63.5 ± 18.7 and 62.9 ± 18.2 years, respectively. The duration of hospital stay among cases was 4.9 ± 1.4 and controls 1.8 ± 1.0 weeks ($p < 0.001$) (Table 1).

2. Site of infection and susceptibility of AB

Lower respiratory tract was the most common site of MDR-AB nosocomial infection (74.8%) followed by urinary tract (11%). Surgical site infection and blood stream infection were equally found at 4.5%. *Acinetobacter baumannii* was 100% resistant to ceftriaxone and susceptible to netilmycin in 36.1% followed by cefoperazone/sulbactam in 17.1%.

Table 1. Characteristics of case and control groups

Variable	Case (n = 155)		Control (n = 310)		p-value
	Number	%	Number	%	
Gender					0.053
Male	83	53.5	195	62.9	
Female	72	46.5	115	37.1	
Age (Years)					0.784
15-40	23	14.9	43	13.9	
41-60	35	22.6	79	25.5	
> 60	97	62.6	188	60.6	
Range	15-95		16-94		
Mean (SD)	63.5 (18.7)		62.9 (18.2)		
Department					0.891
Medicine	100	64.5	198	63.9	
Surgery	55	35.5	112	36.1	
Ward					0.947
General	88	56.7	175	56.4	
Intensive-care	67	43.3	135	43.6	
Length of admission					<0.001
≤ 2 weeks	13	8.4	254	81.9	
> 2 weeks	142	91.6	56	18.1	
Range	1-7		1-5		
Mean (SD)	4.9 (1.4)		1.8 (1.0)		

3. Risk factors for MDR-AB

The results from multivariate analysis, controlling for all variables in the table, demonstrated significant risk factors for MDR-AB nosocomial infection as follows: length of stay > 1 week in hospital prior to MDR-AB nosocomial infection (OR = 2.06; 95%CI 1.09-3.89), indwelling urinary catheter less than 1 week and equal 1 week (OR = 3.13; 95%CI 1.46-6.69) and more than 1 week (OR = 8.24; 95%CI 3.81-17.82), mechanical ventilation less than 1 week and equal 1 week (OR= 3.71; 95%CI 1.96-7.00) and more than 1 week (OR = 5.73; 95%CI 2.96-11.10), central venous line > 1 week (OR = 3.29; 95%CI 1.48-7.31), nasogastric intubations less than 1 week and equal 1 week (OR = 3.24; 95%CI 1.69-6.21) and more than 1 week (OR = 6.22; 95%CI 3.24-11.93) (Table 2). Besides, prior to using antibiotic drug was also a significant risk factor for MDR-AB nosocomial infection which were administration of 3rd, 4th generation cephalosporins (OR = 1.80; 95%CI = 1.04-3.13), metrodazole (OR = 2.59; 95%CI = 1.21-5.56) piperacillin-tazobactam (OR = 4.68; 95%CI = 1.93-11.32) when compared to who did not (Table 3).

Discussion

Infections by antimicrobial resistant organisms have been a major health problem worldwide including Thailand. The impact of these infections, especially in nosocomial infection, is enormous regarding morbidity, mortality, and economic loss. Among bacteria, AB has emerged as a most antimicrobial resistant hospital pathogen[1,2,5,7-12]. The bacterium has been found in pneumonia, urinary tract, and surgical site, the major sites of nosocomial infections[6]. To reduce the prevalence of AB in nosocomial infection, effective preventive measures must be focused on patients with risk factors for the infection[14-18]. The present study was to identity risk factors for AB nosocomial infection in medical and surgical patients in 2005 involving 155 cases of AB nosocomial infection and 310 cases without the infections as control (Table 1). About two-thirds were male, aged over 60 years, and were medical patients. They were relatively severely ill as 43.3 percent were treated in intensive care units where AB was endemic.

Surgery, steroid treatment, and chronic diseases were not significantly associated with AB nosocomial infection (Table 2). However, the infection was found more in patients with indwelling devices: urinary catheter, mechanical ventilation, central venous line, and nasogastric tube. These devices are

Table 2. Association between risk factors and multidrug-resistant *Acinetobacter baumannii* nosocomial infection by multivariate analysis

Risk factors	Crude OR	95%CI	Adjusted OR	95%CI	p-value
Duration of admission prior to infection					
≤ 1 week	1		1		
> 1 weeks	4.14	2.57-6.67	2.06	1.09-3.89	0.025
Steroid treatment					
No	1		1		
Yes	1.74	1.04-2.91	1.53	0.76-3.10	0.233
Surgery					
No	1		1		
Yes	1.70	1.14-2.55	0.93	0.52-1.67	0.817
Urinary catheterization					
No	1		1		
Yes ≤ 1 week	3.67	1.83-7.36	3.13	1.46-6.69	0.033
Yes > 1 week	17.37	8.92-33.82	8.24	3.81-17.82	<0.001
Mechanical ventilation					
No	1		1		
Yes ≤ 1 week	4.50	2.57-7.87	3.71	1.96-7.00	<0.001
Yes >1 week	13.23	7.62-22.97	5.73	2.96-11.10	<0.001
Central venous line					
No	1		1		
Yes ≤ 1 week	3.31	1.79-6.12	1.29	0.61-2.73	0.501
Yes > 1 weeks	9.37	4.80-18.30	3.29	1.48-7.31	0.003
Nasogastric intubation					
No	1		1		
Yes ≤ 1 week	4.81	2.70-8.57	3.24	1.69-6.21	<0.001
Yes > 1 week	14.07	8.11-24.43	6.22	3.24-11.93	<0.001

indispensable for severely ill patients. Improvement in the quality of insertion and care could reduce the risk. Education to medical personnel and enforcement of implementation of infection control measures are essential for the success[12-15].

The infection was associated with certain antimicrobials previously given to patients (Table 3). The antimicrobials lead to selection of resistant bacteria in colonization and subsequent infections in these patients. In the present study, only 3rd and 4th generation cephalosporins, metronidazole, and piperacillin-tazobactam were found to be associated with AB nosocomial infection. Other antimicrobials could have been a risk factor for AB nosocomial infection if more patients had been enrolled.

Conclusion

A case-control study in medical and surgical patients in Siriraj Hospital in 2005 revealed risk factors for AB nosocomial infection. Prolonged admission of more than 2 weeks, use of devices and prior treatment with certain antimicrobials were found to be significant risk factors for the infection. To reduce infection, strict infection control measures must be applied to patients with these risk factors. Education of medical personnel and enforcement of infection control practices are all needed to reduce antimicrobial resistant bacterial nosocomial infection.

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Table 3. Association between antimicrobial used and multidrug-resistant *Acinetobacter baumannii* nosocomial infection by multivariate analysis

Antimicrobials	Crude OR	95%CI	Adjusted OR	95%CI	p-value
Penicillins					
No	1		1		
Yes	2.27	1.15-4.46	1.04	0.41-2.66	0.936
Other Beta-lactam					
No	1		1		
Yes	2.64	1.58-4.39	1.48	0.77-2.85	0.239
3rd-4th Cephalosporins					
No	1		1		
Yes	2.60	1.75-3.86	1.80	1.04-3.13	0.036
Carbapenems					
No	1		1		
Yes	3.77	2.46-5.77	1.36	0.78-2.38	0.284
Aminoglycosides					
No	1		1		
Yes	2.72	1.58-4.71	1.22	0.61-2.46	0.574
Metronidazole					
No	1		1		
Yes	4.22	2.28-7.80	2.59	1.21-5.56	0.014
Macrolides					
No	1		1		
Yes	2.31	1.31-4.08	0.79	0.37-1.69	0.546
Quinolones					
No	1		1		
Yes	2.49	1.56-3.97	0.87	0.46-1.63	0.668
Piperacillin/Tazobactam					
No	1		1		
Yes	7.35	3.60-15.02	4.68	1.93-11.32	0.001
Vancomycin					
No	1		1		
Yes	5.75	3.24-10.18	1.84	0.90-3.75	0.093

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ปัจจัยเสี่ยงของการติดเชื้อดื้อยา *Acinetobacter baumannii* ในโรงพยาบาลศิริราช

กัลยาณี ศุระศรางค์, กุลยา นาคสวัสดิ์, สมหวัง ด่านชัยวิจิตร, กนกรัตน์ ศิริพานิชกร, ดุสิต สุจิรารัตน์, ยงค์ รงค์รุ่งเรือง, ภัทรชัย กีรติสิน

วัตถุประสงค์: *เพื่อศึกษาปัจจัยที่มีความสัมพันธ์กับการติดเชื้อดื้อยา A. baumannii ในโรงพยาบาล*

วัสดุและวิธีการ: *การศึกษาแบบย้อนหลังเพื่อศึกษาปัจจัยที่มีความสัมพันธ์กับการติดเชื้อดื้อยา A. baumannii โดยศึกษาในผู้ป่วยที่เข้ามารับการรักษาในโรงพยาบาลศิริราช ระหว่างวันที่ 1 มกราคม พ.ศ. 2548 ถึง 31 ธันวาคม พ.ศ. 2548 กลุ่มตัวอย่างศึกษาคือ ผู้ป่วยที่ติดเชื้อดื้อยา A. baumannii ในโรงพยาบาลจำนวน 155 คน และกลุ่มควบคุม คือ ผู้ป่วยที่ไม่มีการติดเชื้อในโรงพยาบาลจำนวน 310 คน จับคู่ 1:2 ด้วยหอผู้ป่วย และอายุ*

ผลการศึกษา: *อายุเฉลี่ยในกลุ่มศึกษา 63.5 $\pm$ 18.7 ปี และในกลุ่มควบคุม 62.9 $\pm$ 18.2 ปี ระยะเวลานอนโรงพยาบาลเฉลี่ยในกลุ่มศึกษา 4.9 $\pm$ 1.4 สัปดาห์ และในกลุ่มควบคุม 1.8 $\pm$ 1.0 สัปดาห์ ตำแหน่งของการติดเชื้อดื้อยา A. baumannii ที่พบมากที่สุดคือ การติดเชื้อในทางเดินหายใจส่วนล่าง (74.8%) ความไวของเชื้อ A. baumannii ต่อยาเซฟไตรอะโซน 3.9 % และไวต่อยาเซฟโฟเพอราโซน/ซัลแบกแทม 42.1% ผลการวิเคราะห์ตัวแปรเชิงซ้อน พบว่าปัจจัยที่มีความสัมพันธ์ต่อการเกิดการติดเชื้อดื้อยา A. baumannii ได้แก่ ระยะเวลาที่อยู่ในโรงพยาบาลก่อนการติดเชื้อในโรงพยาบาลมากกว่า 1 สัปดาห์ (OR = 2.06, 95%CI = 1.09-3.89) การใส่สายสวนปัสสาวะ มากกว่า 1 สัปดาห์ (OR = 8.24, 95%CI = 3.81-17.82), ใช้เครื่องช่วยหายใจ มากกว่า 1 สัปดาห์ (OR = 5.73, 95%CI = 2.96-11.10), ใส่สายสวนเข้าหลอดเลือดส่วนกลางมากกว่า 1 สัปดาห์ (OR = 3.29, 95%CI = 1.48-7.31), ใส่สายยางให้อาหารทางจมูกสู่กระเพาะอาหารมากกว่า 1 สัปดาห์ (OR = 6.22, 95%CI = 3.24-11.93) และการรักษาด้วยยาเซฟาโลสปอรินส์รุ่นที่ 3 และ 4 (OR = 1.80, 95%CI = 1.04-3.13), ยาเมโทรนิดาโซล (OR = 2.59, 95%CI = 1.21–5.56) และยาพิเพอราซิริน/ทาโซแบกแทม (OR = 4.68, 95%CI = 1.93-11.32)*

สรุป: *การศึกษาในผู้ป่วยอายุรกรรมและศัลยกรรมในโรงพยาบาลศิริราช พ.ศ. 2548 พบว่า ปัจจัยเสี่ยงต่อการติดเชื้อ A. baumannii ในโรงพยาบาล ได้แก่ การนอนโรงพยาบาลนาน การใส่อุปกรณ์เข้าร่างกาย และการใช้ยาต้านจุลชีพบางขนาน ควรจะเข้มงวดต่อมาตรการป้องกันการติดเชื้อในผู้ป่วยที่มีปัจจัยเสี่ยง การให้การอบรมและการปฏิบัติอย่างถูกต้อง จะช่วยลดการติดเชื้อดื้อยาในโรงพยาบาล*