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Risk factors for mortality in *Acinetobacter calcoaceticus–baumannii* bacteraemia

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ABSTRACT

Objective: To determine the risk factors associated with mortality in *Acinetobacter calcoaceticus–baumannii* (*Acb*) complex blood stream infection. **Methods:** This was an observational study conducted in tertiary care hospital of South India. All patients with blood culture positive for *Acb* complex from January 2008 to December 2009 were included and a standardized abstraction form was used to abstract data. *P* value was calculated by Chi square test. Univariate analysis was done by using 2x2 tables and the variables with P value of <0.1 were further subjected to multivariate analysis. Multivariate analysis was done by logistic regression method. **Results:** After excluding the polymicrobial infections and duplicate isolates from the same patients, 81 cases were included in our study. Out of 81 patients, 20 (24.6%) patients had positive isolate from body secretion other than blood for *Acb* complex, majority were hospitalized in intensive care unit (74%), had indwelling vascular catheters (68%) and were mechanically ventilated (61%). Multi drug resistant phenotypes were seen in 56 (69.1%) isolates and among them 13 (16%) were resistant to carbapenems. Univariate analysis showed renal disease, diabetes mellitus, use of mechanical ventilation and absence of appropriate antibiotic therapy, leucopenia, thrombocytopenia and raised prothrombin time were related to increased mortality in *Acb* complex bacteraemia. However, in multivariate analysis independent risk factors for mortality in *Acb* complex bacteraemia were platelets of less than 1.5 lacks and inappropriate empirical antibiotics. **Conclusions:** Thrombocytopenia and absence of appropriate antibiotics were risk factors associated with mortality in *Acb* bacteraemia. Patients with blood culture showing *Acb* complex bacteraemia with above findings should be attended with aggressive management. Clinician of hospitals with high incidence of *Acb* complex bacteraemia, should predict the chances of such infection even prior to blood culture reports are available, and should initiate appropriate antibiotics according to their institution antibiogram.

1. Introduction

The impact of nosocomial blood stream infection on the outcome of critically ill patients has been extensively studied, with an attributable mortality rate ranging from 19% to 35%[1-4]. Members of the *Acinetobacter calcoaceticus–baumannii* complex (Acb complex) are the predominant *Acinetobacter* in clinical settings, and isolates are usually multi-resistant, complicating therapy and frequently causing outbreaks. Colonization by *Acinetobacter* spp. in healthy people and damaged tissue is common due to the preference for moist environment[5]. It is widely distributed in nature and in the hospital environment causing opportunistic infections in debilitated patients especially in intensive care units[5]. *Acinetobacter* spp. is included the list of six top priority dangerous drug resistant microbes, released by Infectious Disease Society of America[6]. Clinical infections caused by *Acb* complex include pneumonia, meningitis, bacteraemia, soft-tissue infections, surgical site infections, peritonitis, endocarditis, and catheter-related and urinary tract infections[7]. Frequent developments of multiple antimicrobial resistances has enhanced the virulence of this pathogen severely restricting the therapeutic options available for infected patients, thereby increasing the length of stay in intensive care unit (ICU) and mortality[8,9]. As the incidence of *Acinetobacter* blood stream

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infection (BSI) is on the rise, our study aims to determine the risk factors associated with mortality in such cases.

2. Material and methods

We conducted an observational study to determine the risk factors associated with mortality of all patients who had a positive blood culture for *Acb* complex from January 2008 through December 2009 at a tertiary care teaching institute in South India. Data were abstracted using a standardized abstraction form.

2.1. Various definitions

2.1.1. A case of Acb complex sepsis

A case of *Acb* complex sepsis was defined as any patient with clinical symptoms of infection growing *Acb* complex in at least one blood culture bottle. Patients with poly-microbial infections were excluded and patients with only one isolate were included in the study.

2.1.2. Nosocomial bacteraemia

Nosocomial bacteraemia was defined on the basis of the isolation of *Acb* complex from blood cultures 48 h after admission with features of systemic inflammatory response syndrome (SIRS)[10,11].

2.1.3.Colonization

Colonization was defined as the presence of *Acb* complex in secretions or excretions, on mucous membrane, in open wounds or skin without any adverse clinical signs or symptoms. The following clinical characteristics were recorded: Sex, age, duration of hospital stay, need for mechanical ventilation, use of central venous catheter, presence of underlying disease(s), history of prior and appropriate antibiotic therapy, days of admission before index culture, fatal outcome (death) if observed.

2.1.4. Appropriate antibiotics treatment

Appropriate antibiotics treatment was considered if the patient received at least one antibiotic that was sensitive in-vitro with /without other measures like removal of indwelling catheter, regular dressing of wound or surgical drainage.

2.1.5. Prior antimicrobial therapy

Prior antimicrobial therapy was defined as the use of a systemic antimicrobial agent for at least 72 h within the 2 weeks preceding the date of the positive-culture.

2.1.6. Appropriate empirical antibiotic therapy

Appropriate empirical antibiotic therapy was defined as the administration of appropriate therapy soon after index blood culture, *e.g.* within 24-48 h. The primary outcome measure was in-hospital mortality. Institute Ethical committee had approved the study as per international guidelines[12].

2.2. Clinical specimens, Acinetobacter identification and sensitivity testing

For culture 10 mL of blood was collected by aseptic procedures and inoculated into BACTEC™ Plus Aerobic/F or BacT/Alert 3D bottles and was placed in the BACTEC 9240 or BacT/Alert 3D blood culture instrument with in 2 h of collection. Identification and susceptibility testing was done either manually using standard biochemical test or by automated ID 32GN Mini API system (BioMerieux, Inc., St. Louis, MO). Specific phenotypic characteristics include the appearance of cocci or coccobacilli on Gram stain, the ability to grow on MacConkey agar, and resistance to penicillin. Major genus characteristics include the inability to ferment glucose (non-fermenter), lack of oxidase production (oxidase negative), and non-motility. Antibiotic sensitivity was determined using the disc diffusion method, according to the Clinical and Laboratory Standards Institute guidelines[13]. The microorganism was defined as MDR if it was resistant to more than three of the following eight antimicrobial agents: ampicillin/sulbactam, aztreonam, ceftazidime, ciprofloxacin, gentamicin, imipenem, piperacillin and trimethoprim/sulfamethoxazole[14].

2.3. Statistical analysis

Distribution and frequencies of all important variables were done using descriptive statistics. All P values were based on 2-tailed tests. Reported P values are for the chi-square test unless stated otherwise. Univariate analysis was done to test association between prognostic variables and response variables. Variables with P value <0.1 were included in multivariate logistic regression using enter method. A P value of <0.05 was considered to be statistically significant. Kaplan-Meir methods were used for the survival analyses from the day of hospital admission. Statistical analysis was conducted using SPSS software (SPSS-11.0 version).

3. Results

3.1. Base line demographics

During the two year study period our clinical microbiology laboratory received 28 773 blood culture bottles of which 8.8% (2 552) were found to be positive. Among the 2 552 isolates 126 (4.9%) were *Acb* complex. After excluding the polymicrobial infections and duplicate isolates from the same patients 81 cases were included in our study. Patients' characteristics are shown in (Table 1).

3.2. Duration of hospital stay prior to index culture

Table 1.
Base line demographics of the study cohort.

Variable		n=81 (%), range
Age (year)		52.6(1-95)
Gender	Male	58(71.6)
	Female	23(28.4)
Median length of hospital stay(days)		14(1-87)
Mean duration of hospitalization before septicemia(days)		10 (0-67)
Location of admission	Intensive care unit setting	60(74.1)
	Non ICU setting	21(25.9)
Total duration of ICU stay (days)(n=60)		5(0-64)
Procedures	Mechanical ventilation	50(61.7)
	Surgery(CVS/GI/CNS)	35(43.1)
	Central venous catheter	39(48.1)
	Urinary catheter	54(66.7)
Underlying diseases	Diabetes mellitus	30(37.0)
	Cardiac diseases	19(23.5)
	Renal impairment	17(21.0)
	Chronic obstructive lung disease	17(21.0)
	Stroke	10(12.3)
	Malignancy	12(14.8)
Primary source of infection	Not identified	60(74.07)
	Sputum/endotrachal suction/ bronchoalveolar lavage	18(22.20)
	Pleural effusion/Ascites	2(2.40)
Prior antibiotic therapy(n=60)	Cephalosporins	25(41.6)
	Piperacillin+tazobactem	22(36.6)
	Cefoperazone+salbactum	14(23.3)
	Fluroquinolone	9 (15.0)
	Imipenem+cilstatin	8(13.3)
	Augmentin	3(5.0)
	Metrogyl	3(5.0)
	Aminoglycosides	5(8.33)
	Ampicillin	4(6.66)
	Vancomycin	1(1.66)
	Linezolid	3(5.0)
	Two antibiotics	18(30.0)
Appropriate empirical antibiotics	Received	42(52.0)
	Not received	39(48.1)
Fatal outcome	Death	36(44.4)
Acinetobacter sensitivity	Non MDR AB	25(30.1)
	MDR AB	56(69.1)
	CRAB	13(16.0)

The mean duration of stay in hospital before index culture came positive for *Acb* complex was 10 days (range 0-67 days).

3.3 Monthly distribution of Acb bacteraemia

The monthly incidence did not show any particular pattern and cases were uniformly distributed throughout the year.

3.4 Simultaneous Acb isolation from body fluid/sputum

Of the 81 cases 68% grew *Acb* complex in only one blood culture bottle, 30% in two bottles and in only two cases three bottles (from two sets of blood culture) were positive. *Acb* complex was also seen in 22.2% cases from sputum or endotracheal aspirate. In one case, *Acb* was isolated from pleural fluid and the other simultaneously from bile (from liver transplant patient) as well as peritoneal fluid. Presence of central venous catheter was documented in 39 (41.8%) cases, but only four catheter tips were sent for culture and none of them grew *Acb* complex.

Table 2.
Clinical characteristic of patients with ACB bacteraemia and their relationship with mortality (n=81).

Variable	Factor	No of patient's with fatal outcome(n=36)	Odd's ratio (95% confidence interval)	P value
Age	>52	9(21)	2.625(1.010-6.822)	0.037
	<52	27(54)		
Gender	M	24(58)	1.545(0.585-4.080)	0.378
	F	12(23)		
Old stroke	No	34(71)	0.272(0.054-1.372)	0.272
	Ye	02(10)		
Cardiac failure	No	27(62)	1.167 (0.416-3.271)	0.769
	Ye	09(19)		
End stage renal disease	No	22(64)	8.909(2.311-34.346)	<0.001
	Ye	14(17)		
Chronic obstructive Pulmonary disease	No	28(64)	1.143(0.391-3.341)	0.807
	Ye	8(17)		
Diabetes Mellitus	No	15(51)	5.600(2.089-15.014)	<0.001
	Ye	21(30)		
Malignancy	No	31(69)	0.876(0.253-3.031)	0.545
	Ye	5(12)		
Mechanical ventilation	No	7(31)	4.735(1.721-13.026)	0.002
	Ye	29(50)		
Appropriate empirical antibiotics	No	23(39)	0.303(0.110-0.832)	0.018
	Ye	13(42)		
Multidrug resistance	No	11(25)	1.026(0.397-2.652)	0.576
	Ye	25(56)		
Carbapenem resistance	No	31(68)	0.746(0.221-2.514)	0.436
	Ye	5(13)		

3.5 Antibiotic susceptibility

Antibiotic susceptibility testing of the 81 non-duplicate *Acb* complex isolates by Kirby-Bauer disk diffusion method showed that 74% (40/81) were multi-drug resistant (MDR). Co-resistance was least in carbapenems (n=13, 16%) followed by cefoperazone/sulbactam (n=23, 28%), piperacillin / tazobactam (n=27, 33%), ciprofloxacin (n=44, 54%), gentamicin (n=45, 56%), piperacillin (n=51, 63%), ceftazidime (n=53, 66%) and cefoperazone (n=63, 77%). All the isolates were susceptible to colistin.

3.6 Risk factors for mortality in Acb bacteraemia

The patients were often admitted to the ICU (74%), and

mechanically ventilated (61%). Appropriate empirical antibiotics were administered in 42 (52%) cases of which 13 (31%) died. Of the 39 (48%) patients who were administered inappropriate empirical antibiotics 22 (56.4%) died. The patients who died in spite of receiving appropriate empirical antibiotic therapy were more likely >50 years of age (11/13), had suffered a cerebrovascular accident (7/13) and were diabetic (5/13). Table 2 shows the univariate analysis of different clinical characteristics and their association with *Acb* complex bacteraemia. Age >52 years (P=0.037), diabetes mellitus (DM) (P<0.001), end stage renal disease (ESRD) (P<0.001), inappropriate empirical antibiotic treatment (P=0.018) and mechanical ventilation (P=0.002) were found to be associated with poor outcome. Other variables like chronic obstructive pulmonary disease (COPD), cardiac disease, history of surgical procedures, carbapenem resistance did not show statistically significant association with mortality. Laboratory parameters like platelet counts, total counts, serum creatinine, blood urea, and prothrombin time and their association with mortality were checked with univariate analysis (Table 3) and it showed low platelets <1.5 lacs/ mm^3 (P=0.041) and inappropriate empirical antibiotic therapy (P=0.027) were found to have significant association with mortality (Table 4). Survival analysis was done using Kaplan-Meier methods, which showed increased mortality in patients with platelets less than 1.5 lacs/mm^3 and who received inappropriate antibiotics (Figure 1 and 2). The mortality difference appears to occur early on (prior to day 14) as shown in curves which also support conclusion that inappropriate initial antibiotic therapy may be independently associated with mortality.

Table 3.
Laboratory parameters of patients with Acb bacteraemia and their relationship with mortality (n=81).

Laboratory investigation	No of patients with fatal outcome(total no)	P value (OR, 95% CI)
Total white blood cell		
count< 4 000 or >11 000	19(42)	0.530(0.9, 0.4-2.24)
4 000-11 000	17(39)	
Neutrophil		
>70%	17(33)	0.202(1.3, 0.8-2.1)
<70%	19(48)	
Platelets		
>1.5 lakh	20(59)	0.002(2.424, 1.2-4.9)
<1.5 lakh	16(22)	
Blood urea		
<40 mg/dL	11(39)	0.001(4.7, 1.8-12.4)
>40 mg/dL	24(37)	
S. creatinine		
<1.4 units	20(59)	<0.001(7.8, 2.3-26.4)
>1.4 units	16(20)	
Prothrombin time		
<15 seconds	7(26)	0.01(3.78, 1.31-10.8)
>15 seconds	25(43)	

Table 4.
Multivariate analysis (Logistic regression method).

Variable	OR (95% confidence interval)	P value
Age	1.308(0.312-5.485)	0.154
Diabetes mellitus	2.445(0.501-11.537)	0.548
End stage renal disease	1.860(0.190-18.180)	0.583
Ventilator support	4.430(0.894-21.944)	0.051
Appropriate antibiotics given	0.212(0.056-0.807)	0.027
Platelet count< 1.5 lac	3.773(0.859-16.572)	0.044
S.creatinine.1.5	1.717(0.205-14.367)	0.733
Prothrombin time> 15 seconds	2.268(0.535-9.617)	0.567
Blood urea >40 mg/dL	2.349(0.538-10.257)	0.737
Carbapenem resistant *Acinetobacter*	1.301(0.201-8.433)	0.982

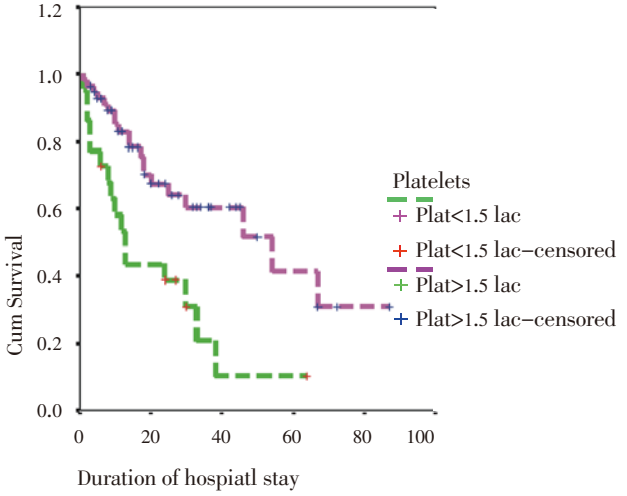

Figure 1. Effect of decreased platelets on survival, patients with platelets less than 1.5 lacs/mm^3 and patients with platelets greater than 1.5 lacs/mm^3.

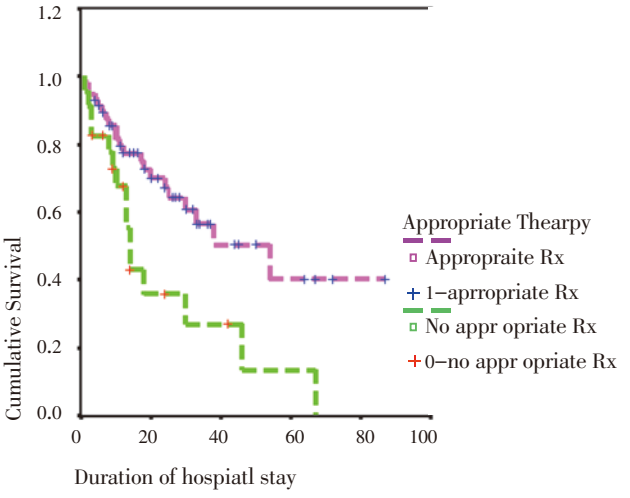

Figure 2. Effect of appropriate antibiotics on survival in Acb complex bacteremia, patients who received appropriate therapy and who did not receive appropriate antibiotics.

4. Discussion

Nosocomial bacteraemia caused by *Acinetobacter* species is

of great concern in critically ill patients, and the risk factors for this infection related mortality are not well established. This was an observational study to determine risk factors for mortality associated with *Acinetobacter* species bacteraemia. Univariate analysis showed renal disease, diabetes mellitus, use of mechanical ventilation and absence of appropriate antibiotic therapy were associated with increased mortality. Patients with DM and ESRD frequently visit hospitals for treatment of complications like diabetic foot and dialysis respectively. Therefore these patients in addition to being immunocompromised have all the risk factors for *Acb* complex acquisition like prior use of multiple classes of antibiotics, invasive surgical procedures and frequent admission to the hospitals. The average duration of hospital stay was 14 days and was longer in case Carbapenem resistant *Acb* complex bacteraemia. The average duration of hospital stay before positive index culture was 10 days. Similarly other studies have documented a hospital stay of more than one week with prior use of broad spectrum antibiotics as a significant risk factor for acquisition of *Acb* complex[5].

In present series, most of the patients were in ICU and were mechanically ventilated. These are the two common risk factors reported for *Acinetobacter* bacteraemia in previous studies[16-18].As documented previously, in our study also history of previous hospitalization and previous antimicrobial therapy were detected as important predisposing factors for *Acinetobacter* acquisition[19,20]. A recent history of surgical procedure was documented in 43% cases, consistent with previous studies which have shown an increase of *Acinetobacter* acquisition from various invasive procedures[14].Risk of secondary bacteraemia due to *Acinetobacter* increases many folds with tracheobronchitis and pneumonia[19-21].We recorded 39% mortality in patients with carbapenem resistant *Acb* complex which were consistent with similar observations[22,23]. Appropriate empirical antimicrobial therapy significantly reduced the mortality attributed to *Acb* complex bacteraemia which is similar to other reports[23,24].Despite of appropriate antibiotics 31% of patients had fatal outcome this can be due to underlying disease or co-morbidity. In addition, we have to say that mortality is crude mortality and not attributable mortality due to *ACB* complex bacteraemia.

Antibiotic susceptibility profile of *Acinetobacter* spp. differs in different countries and even among the wards of a given hospitals. With the prevalence of ESBL producing Enterobacteriaceae reaching epidemic proportions in many Indian medical centers, carbapenems are being extensively used creating an environment conducive for emergence of carbapenem resistant *Acinetobacter* isolates. [25].The prevalence of MDR *Acinetobacter* in our study was 69% which was similar to previous study, [26].while carbapenem resistance was 16%. The most active agent against the carbapenem resistant isolates in our study was cefoperazone/sulbactam with a susceptibility rate of 49%. Yun-Song Yu et.al studied 45 carbapenem isolates and found that cefoperazone/sulbactam and ampicillin/sulbactam were the only active agents, with a susceptibility of 63% and 43.5% respectively[15]. This may be due to the unique activity of sulbactam against *Acinetobacter* spp. sulbactam acts synergistically with cephalosporins in the treatment of infections caused by such isolates[27]. Last but not the least, efforts to remove invasive devices and equipment such as endotracheal tube or central venous catheter as soon as possible are needed to prevent development of MDR AB bacteremia among the colonized patients[28-30].

The antibiotics available for the carbapenem resistant *Acb* complex septicemia are very few. Therefore, efforts should be taken to reduce incidence of *Acb* bacteraemia, which starts with the primary measure like reducing intrinsic contamination and colonization of medical equipment or devices used for monitoring and therapy of patients, and hand hygiene to prevent cross infection in the ICU.

Strength of the study was its adequately large sample size to say the results statistically significant. The study also addressed all the issues related to risk factors of mortality in *Acb* complex septicemia in extensive detail. In era of pan resistant micro organism, this study will help intensive care physician for identifying the risk factors for *Acb* complex septicemia as well as risk factors associated with increased mortality. Accurate data retrieval was possible, as our hospital is equipped with electronic medical record maintenance system.

Limitation is it was a retrospective single center study. Our hospital is a tertiary care hospital which has 213 ICU beds, which is a huge number. That might have affected the incidence of *Acb* complex bacteremia in present study and results may not be generalized.

The data may be helpful for planning the future multicentre study for more appropriate documentation of incidence and risk factors of *Acb* complex bacteremia. Due to financial constraints molecular based study on *Acb* for identifying the different strains was not conducted. To find out the virulent strain to start appropriate antibiotics may be future area of interest.

Present study showed that thrombocytopenia and absence of appropriate antibiotic therapy were associated with mortality. Early intervention and appropriate empirical antibiotics and setting with high prevalence of *acinetobacter* will helpful in preventing mortality.

Conflict of interest statement

We declare that we have no conflict of interest.

References

[1] Prashanth K, Badrinath S. Nosocomial infections due to *Acinetobacter* species: Clinical findings, risk and prognostic factors. *Indian J Med Microbiol* 2006;**24**:39-44.

[2] Cisneros JM, Rodríguez-Baño J, Fernández-Cuenca F, Ribera A, Vila J, Pascual A, et al. Risk-factors for the acquisition of imipenem-resistant *Acinetobacter* baumannii in Spain: a nationwide study. *Clin Microbiol Infect* 2005; **11**: 874-879.

[3] Baran G, Erbay A, Bodur H, Öngürü P, AkIncI E, Balaban N, et al. Risk factors for nosocomial imipenem-resistant *Acinetobacter* Baumanni infections. *Int J Infect Dis* 2008; **12**:16-21.

[4] Jung JY, Park MS, Kim SE, Park BH, Son JY, Kim EY, et al. Risk factors for multi-drug resistant *Acinetobacter* baumannii bacteremia in patients with colonization in the intensive care unit. *BMC Infect DiS* 2010; **10**:228.

[5] Joshi SG, Litake GM, Satpute MG, Telang NV, Ghole VS, et al. Clinical and demographic features of infection caused by *Acinetobacter* species. *Indian J Med Sci* 2006; **6**0:351-60.

[6] Talbot GH, Bradley J, Edwards JJ, Gilbert D, Scheld M, Bartlett JG. Bad bugs need drugs: an update on the development pipeline from the antimicrobial availability task force of the infectious diseases society of america. *Clin Infect Dis* 2006; **42**: 657-668.

[7] Allen DM, Hartman BJ. *Acinetobacter* species. In: Mandell GL, Bennett JE, Dolin R, eds. Principles and practice of infectious diseases. Philadelphia: Churchill Livingstone; 2000, p. 2339-2344.

[8] Maragakis L, Perl TM. *Acinetobacter* baumannii: epidemiology, antimicrobial resistance, and treatment options. *Clin Infect Dis* 2008; **46**:1254-1263.

[9] Falagas ME, Bliziotis IA, Siempos I. Attributable mortality of *Acinetobacter* baumannii infections in critically ill patients: a systematic review of matched cohort and case-control studies. *Critical care* 2006; **10**:48.

[10] American Thoracic Society documents: Guidelines for the management of adults with hospital acquired pneumonia, ventilator associated pneumonia and health care associated pneumonia. *Am J Respir Crit Care Med* 2005; **171**:388-416.

[11]. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions of nosocomial infections. In: Olmsted RN, ed:APIC Infection Control and Applied Epidemiology: Principles and Practice. St. Louis: Mosby; 1996, p. A-1-A-20..

[12] Document of Public welfare department of health and human services United States of America: Code of federal regulations. Available at http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.101, 2009.

[13] Clinical and Laboratory Standards Institute: Methods for Dilution Antimicrobial Susceptiblity Tests for Bacteria That Grow Aerobically; Approved Standard-8th Edition. Clinical and Laboratory Standards Institute 2008; **29**:M07-A08.

[14] Kwon KT, Oh WS, Song J, Chang H, Jung S, Kim S, et al. Impact of imipenem resistance on mortality in patients with *Acinetobacter* bacteraemia. *J Antimicrobiol Chemother* 2007; **59**:525-530.

[15] Yu YS, Yang Q, Xu XW, Kong HS, Xu GY, Zhong BY. Typing and characterization of carbapenem-resistant *Acinetobacter calcoaceticus*-baumannii complex in a Chinese hospital. *J Med Microbiol* 2004;**53**:653-656.

[16] Luna CM, Aruj PK. *Nosocomial Acinetobacter Pneumonia*. *Respirology* 2007;**12**:787-797.

[17] Cisneros-Herreros JM, Garnacho-Montero J, Pachon Ibanez ME. Nosocomial Pneumonia due to *Acinetobacter* baumannii. *Enferem Infecc Microbiol Clin* 2005;**23**:46-51.

[18] Robenshtok E, Paul M, Leibovici L, Fraser A, Pitlik S, Ostfeld I, et al. The significance of *Acinetobacter* baumanni bacteremia compared with Klebsiella Pneumoniae bacteremia: Risk factors and outcomes. *J Hosp Infect* 2006;**64**:282-7.

[19] Jang TN, Lee SH, Huang CH, Lee CL, Chen WY: Risk factors and impact of nosocomial *Acinetobacter* baumannii bloodstream infections in the adult intensive care unit: a case-control study. *J Hosp Infect* 2009; **73**:143-150.

[20] Shih M, Lee N, Lee H, Chang C, Wu C, Chen P, et al. Risk factors of multidrug resistance in nosocomial bacteremia due to *Acinetobacter* baumannii: a case-control study. Journal of Microbiology, *Immunol Infect* 2008; **41**:118-123.

[21] Corbella X, Montero A, Pujol M, Domnguez MA, Ayats J, Argerich MJ, et al. Emergence and rapid spread of carbapenem resistance during a large and sustained hospital outbreak of multiresistant *Acinetobacter* baumannii. *J Clinical Microbiol* 2000; **38**:4086-4095.

[22] Chen HP, Chen TL, Lai CH, Fung CP, Wong WW, Yu KW, et al. Predictors of mortality in *Acinetobacter* baumanni bacteremia. *Microbiol Immunol Infect* 2005;**38**: 127-36.

[23] Zakuan ZD, Mohd NS, Harun A. Risk factors and outcomes of imipenem-resistant *Acinetobacter* blood stream infection in North-eastern Malaysia. *Asian Pacific J Trop Biomed* 2011;**1**:313-315.

[24] Erbay A, Idil A, Gözel MG, Mumcuoglu I, Balaban N. Impact of early appropriate antimicrobial therapy on survival in *Acinetobacter* baumannii bloodstream infections. *Int J Antimicrob Agents* 2009; **34**: 575-579.

[25] Kumarasamy KK, Toleman MA, Walsh TR, Bagaria J, Butt F, Balakrishnan R, et al. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and theUK: a molecular, biological, and epidemiological study. *Lancet Infect Dis* 2010;**10**:597-602.

[26] Lahiri KK, Mani NS, Purai SS. *Acinetobacter* spp. as nosocomial pathogens: Clinical significance and antimicrobial sensitivity. *Med J Armed Forces India* 2004;**60**:7-10.

[27] Lautenbach E, Synnestvedt M, Weiner MG, Bilker WB, Vo L, Schein J, *et al*. Epidemiology and impact of imipenem resistance in *Acinetobacter* baumannii. *Infect Control Hosp Epidemiol* 2009; **30**:1186-1192.

[28] Falagas ME, Bliziotis IA, Siempos I. Attributable mortality of *Acinetobacter baumannii* infections in critically ill patients: a systematic review of matched cohort and case-control studies. *Critical Care* 2006; **10**(2):R48-R48.

[29] Erbay A, Idil A, Gzel MG, Mumcuoğlu I, Balaban N. Impact of early appropriate antimicrobial therapy on survival in *Acinetobacter baumannii* bloodstream infections. *Int J Antimicrob Agents* 2009; **34**(6):575-579.

[30] Metan G, Sariguzel F, Sumerkan B. Factors influencing survival in patients with multi-drug-resistant *Acinetobacter* bacteraemia. *European J Int Med* 2009; **20**(5):540-544.