International Journal of Research in Medical Sciences
Pal N et al. Int J Res Med Sci. 2017 Aug;5(8):3620-3625
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20173574

Original Research Article

Extreme drug resistant *A.baumannii* associated with CLA-BSI in Kanpur

Nidhi Pal, R. Sujatha*

Department of Microbiology, Rama Medical College Hospital and Research Center, Kanpur, Uttar Pradesh, India

Received: 12 June 2017
Accepted: 08 July 2017

***Correspondence:**
Dr. R. Sujatha,
E-mail: drsujatha152@gmail.com

ABSTRACT

Background: Nosocomial bloodstream infection on the critically ill patients has been associated with high mortality. Central venous catheters (CVC) have become essential in the management of patients who are critically ill and those who require long-term medical care. This study was conducted to determine the Central line associated blood stream infections (CLA-BSIs) due to *A.baumannii* its risk factors and antibiotic resistant patterns.
Methods: A total of 52 samples (blood or central line tip) were received from patients with a clinical diagnosis of sepsis after central venous catheterization. The semi quantitative method was used for catheter tip culture. Bacterial identification and antibiotics resistant pattern was performed by Standard microbiological protocol.
Results: Of 52 test samples (blood or central line tip), 2 pathogenic strains were isolated from blood, 2 strains of *A.baumannii* isolated from catheter tips were colonizer and 3 strains of *A.baumannii* were pathogenic which caused CLA-BSI. The rate of CLABSI due *A.baumannii* was 11.11 per 1000 catheter days. All *A.baumannii* were extreme drug resistant (XDR). They only sensitive for polymyxins and tegicyclines.
Conclusions: Central venous catheters are increasingly being used in critical care and have been directly related to patient mortality and morbidity. Microbiological surveillance may guide management of multidrug resistant isolates and its complications. Proper infection control practices can reduce the nosocomial infection rate.

Keywords: *A.baumannii*, Antimicrobial resistant pattern, CLA-BSI, Risk factors

INTRODUCTION

The clinical impact of nosocomial bloodstream infection on the critically ill patients has been associated with high mortality.[1] *Acinetobacter baumannii* has recently emerged as a leading cause of nosocomial bloodstream infections in the intensive care unit (ICU) and associated with high mortality.[2,3]

The most common sources of bacteremia are invasive procedure i.e. infected intravascular and respiratory catheters and tubes others like surgical wounds, burns are also sources of bacteremia but to a lower extent.[4] Central venous catheters (CVCs) are essential in the management of critically ill patients for the delivery of medication, parenteral nutrition. Frequent use of CVCs may be associated with blood stream infection.

Central line associated bloodstream infections (CLA-BSI) results from bacterial colonisation that may lead to significant clinical problem. The management of CLA-BSI due to *A.baumannii* was difficult because of its extreme capacity to acquire resistant against antimicrobial agents.[5]

Therefore, routine evaluation of BSI infections are necessary to control infections. Hence this study was aimed to determine CLA-BSI due to *A.baumannii.*

METHODS

This observational study was conducted to determine the CLA-BSI due to *A.baumannii* and its antibiotic resistant pattern from October 2015 to January 2017 at tertiary care hospitals in Kanpur, North India. In the present study total 52 test cases, admitted in intensive care units with intravascular catheters and clinical manifestations, were included. Patients with fever prior to catheter placement were excluded from this study. Test cases were, any patients with intravascular catheter suspected for septicemia; with clinical symptoms were included. Another 50 cases were also observed as a controls for other than *A.baumannii*, admitted in intensive care units with intravascular catheters and clinical manifestations.

Nosocomial bacteremia due to A.baumannii

Nosocomial bacteremia was defined on the basis of the isolation of *A.baumannii* from blood cultures 48 hours after admission with features of systemic inflammatory response syndrome (SIRS).[6]

For suspected Central line associated bloodstream infection (CLA-BSI) draw one set through device and one set from a separate venipuncture. Cultures from both line and blood must be positive for same organism with clinical signs and symptoms and no other recognized source. A positive culture from the line only is probably a contaminant and should not be treated. Preferred Criteria for CR-BSI:

- Differential period of central line culture versus peripheral blood culture positivity > 2 hours
- Simultaneous quantitative blood cultures with a ≥5:1 ratio central line versus peripheral blood culture
- Draw one set through device and one set from a separate venipuncture for routine blood culture.[7]

Device associated infection rate was defined as the no. of device associated infections per 1000 device days. The microorganism was defined as Multidrug Resistant (MDR) if the isolate was resistant to at least three classes of antimicrobial agents-all penicillins and cephalosporins (including inhibitor combinations), fluroquinolones, and aminoglycosides.[8]

The microorganism was defined as Extreme drug resistant (XDR) if the isolate was resistant all penicillins and cephalosporins (including inhibitor combinations), fluroquinolones, and aminoglycosides including Carbapenems.[8]

Clinical specimen's collection and processing

Blood samples and tips of central lines were collected aseptically from the patients.

For blood culture, from adult 10 ml, children 5 ml, and neonates 1 ml of blood was collected by aseptic procedures and inoculated into BHI Broth (Hi Media, Mumbai, India), 70 ml and 20 ml bottles respectively and incubate it. All blood cultures were processed in laboratory using standard procedure by conventional method. After 24 hrs blood culture samples were sub-cultured onto Blood agar and Mac-Conkey agar to look for growth. From the obtained growth, isolated colonies were used for the differentiation of organism and antibiotic sensitivity according to CLSI guidelines, and no growth plates were incubated for further 24 hrs, subcultures from blood culture bottles were done on 2nd, 4th and 6th day, Samples were reported as no growth after 7 days of aerobic incubation.[9]

For central line tip culture, tip processing was done by Maki's Roll over plate method.[10] Briefly, before removing tip the catheter skin was cleaned with 70% alcohol. The proximal end of tip or catheter was held and carefully removed from the patient with a sterile instrument, taking care to avoid contact with the skin and cut approx 2-4 cm segment from tip and placed in sterile container. Semi quantitative culture method was used by rolling the tip across an agar plate; the presence of >15 colonies along with the same organism isolated from peripheral blood with clinical signs and symptoms.[9] Isolated colonies were identified and antibiotic sensitivity testing was performed as per standard microbiological protocol.

The following clinical characteristics were recorded: Sex, age, duration of hospital stay, mechanical ventilation, use of central venous catheter, presence of underlying disease(s), and history of prior antibiotic therapy.

RESULTS

Table 1: Demographic profile of study population.

Demographic profile	Patients with suspected bacterimia (test group) n=52
Age (mean±SD)	51.57±18.89
<30	7
31-60	31
<60	14
Gender	
Male	34
Female	18
ICU stay duration (mean±SD)	12.098±5.426
Device index (mean±SD)	8.69±3.91
Prior hospitalization	Yes (36)

During the 16 month study period total of 52 samples were received from suspected case of nosocomial bacterimia and a total of 13.46% (n=7) were found to be positive for *A.baumannii*. Twenty-five blood samples were received from bacteremia suspected patients. Only 2 case acquired nosocomial *A.baumannii* blood stream infection. Out of 27 cases were on central venous

catheter, were cultured for bacterial growth, only 5 were showed growth for *A.baumannii.* Of 5 *A.baumannii*, only 2 were colonizer and rest 3 *A.baumannii* was associated with CLA-BSI. The rate of CLA-BSI was 11.11 per 1000 device days. The mean device index in the whole population was 8.69±3.91. The index was higher in patients with *A.baumannii* bacteremia than rest of the patients. Patient's demographic profile has been shown in Table 1.

The risk factors among patients who had *A.baumannii* bacteremia with rest of the patients, multiple risk factors were associated with *A.baumannii* bacteremia acquisition in the univariate analysis (Tables 2).

Table 2: Clinical characteristic of patients with bacteraemia.

	Patients with *A.baumannii* bacterimia (test group) n=5	Patient with other than *A.baumannii* associated bacteremia (control group) n=15	Odd ratio (95% CI)	P-value
Age (mean ± SD)	44.66±25.838	44.25±27.90		
<50	1	8	1.5238 (0.2498 to 9.2953)	0.6480
>51	4	7		
Gender				
Male	3	10	0.2353 (0.0651 to 0.8500)	0.0272
Female	2	5		
ICU stay duration (mean ± SD)	11.2±4.207	10.93±5.13		
>11 days	4	7	4.5714 (0.4088-51.1403)	0.2173
Device (mean ± SD)				
Central line duration	8.8±3.962	9.71±4.63	-	-
Device index	1.60±0.77	1.32±0.69	-	-
Invasive procedure				
Abdominal drain	1	2	1.6250 (0.1149 to 22.9821)	0.7194
Arterial catheter	1	2	1.6250 (0.1149 to 22.9821)	0.7194
Central venous	5	10	5.7619 (0.2666 to 124.5497)	0.2641
Catheter	5	5	21.0000 (0.9715-453.9372)	0.0522
Mechanical ventilation	4	9	2.6667 (0.2365 to 30.0678)	0.4275
Nasogastric tube	5	13	2.0370 (0.0835 to 49.6844)	0.6624
Peripheral venous catheter	5	15	0.3548 (0.0063 to 20.1420)	0.6151
Urinary catheter				
Apache score II	23.42±5.53	18.78±2.8	-	-
Co-morbidity			16.0000 (1.2741 to 200.9262)	0.0317
COPD	4	3		
Hypertension	4	10	2.0000(0.1743 to 22.9502)	0.5777
Diabetes	3	5	3.0000 (0.3723 to 24.1719)	0.3021
Cerebral injury	2	4	1.8333 (0.2192 to 15.3335)	0.5759
Renal disease	5	7	12.4667 (0.5862 to 265.1127)	0.1057
Immunosuppresion (prior surgery etc.)	4	4	11.0000 (0.9284 to 130.3297)	0.05
Prior hospitalization	5	4	28.1111 (1.2747 to 619.9333)	0.0345
Prior use of antibiotics	5	11	4.3043 (0.1952 to 94.9236)	0.3551

All the 5 patients with bacteremia were died with the mortality rate 100% while the patients who had bacteremia without *A.baumannii* isolates was 33.3% (Figure 1).

Antibiotic susceptibility testing of the 7 non-duplicate *A.baumannii* isolates by Kirby-Bauer disk diffusion method showed that 85.71% (6/7) were extreme-drug resistant (XDR). All the isolates were susceptible to polymyxins and tigycyclines (Table 3).

Table 3: Antibiotic susceptibility pattern.

	A.baumannii associated with nosocomial bacteremia					Colonizer	
	AB1	**AB2**	**AB3**	**AB4**	**AB5**	**AB6**	**AB7**
PI	R	R	R	R	R	R	R
A/S	R	R	R	R	R	R	R
PIT	R	R	R	R	R	R	R
CFS	R	R	R	R	R	R	R
CTX	R	R	R	R	R	R	R
CTR	R	R	R	R	R	R	R
AK	R	R	R	R	R	R	S
GEN	R	R	R	R	R	R	R
CIP	R	R	R	R	R	R	R
LE	R	R	R	R	R	R	S
IMP	R	R	R	S	R	R	R
PB	S	S	S	S	S	S	S
CL	S	S	S	S	S	S	S
TGC	S	S	S	S	S	S	S

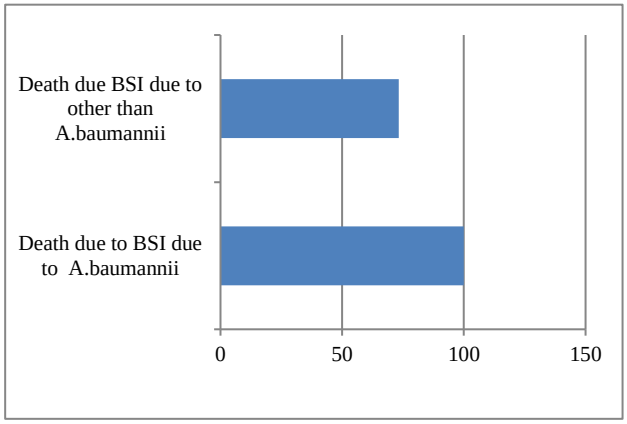

Figure 1: Mortality rate due to *A.baumannii* bacterimia.

DISCUSSION

This prospective study determines the nosocomial bacteremia especially CLA-BSIs due to *A.baumannii* and its antimicrobial resistant pattern. In this study total of 52 samples were received from suspected cases of nosocomial bacteremia and a total of 13.46% (n=7) were found to be positive for *A.baumannii*.

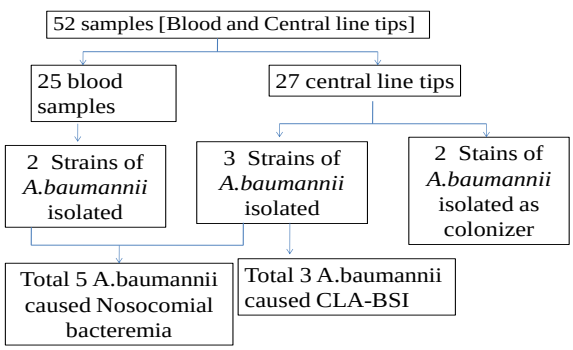

Figure 2: Result scheme of the study.

Among seven isolated *A.baumannii* only 5 were associated with nosocomial bacteremia, Therefore the incidence of nosocomial bacteremia due to *A.baumannii* was 9.62%. This results were comparable to other studies who reported 13.7%, 12.2% and 10.78% of *A.baumannii* from blood.[10-12] While H. Wisplingh off et al. found 1.6% blood stream infection due *A.baumannii* from ICU patients this result was lesser than the present study.[13] Proper aseptic sample collection and better diagnostic methods could be a reason for increased rate of isolation. In this study, male patients were more infected in the both the test and control groups. Age group patients >51 were acquired nosocomial bacteremia.

In the present study, out of 52 cases suspected for bacteremia, 27 patients were on central line catheter and only in 3 cases central line as well as peripheral blood culture show similar isolates. Hence 3 cases were considered as CLA-BSI and rate of CLA-BSI due to *A.baumannii* was 11.1% per 1000 catheter days. BSI was diagnosed by monitoring central venous catheter culture as well as peripheral blood culture along with clinical correlation. Clinically the most common sign associated with the *A.baumannii* bacteremia was fever which occurred in all the bacteremia suspected patients. Hypothermia occurred in none of the patients. The mean maximum temperature was 40.3°C. The mean leukocyte count was 16.7 x 109 leukocyte/L.

Zhou HY et al documented that at least four invasive procedures frequently performed in ICU, that elevated the risk of *A.baumannii* nosocomial bacteremia: Central venous catheter, Urinary catheter, mechanical ventilation and nasogastric tube use.[14]

Consequences of over diagnosis of sepsis: inappropriate use of antibiotics, increases costs, risk of adverse drug reactions, selects for resistant microbial flora increase morbidity and mortality. Incorrect diagnosis can distract a clinician from finding and treating the true cause of a patient's clinical deterioration. Soufir L et al found 5.3 bloodstream infections occur per thousand days of central venous catheter insertion.[15] Apostolopoulou E et al reported 37.8% CLA-BSI and there were no. of studies not reporting *A.baumannii* as a causative agent of CLA-BSI.[16] Khanna V et al reported only 4% of CLA-BSI was due *A.baumannii*.[17] High CLABSIs can be prevented by use of appropriate hand hygiene, aseptic skin preparation, full barrier precautions, the avoidance of femoral catheters, the removal of unnecessary catheters as early as possible, comprehensive educational programs for staff, and in some instances use of antiseptic- or antibiotic-impregnated catheters.[18] The mean device index in the whole population was 8.69±3.91. The index was higher in patients with A. bacterimia than rest of the patients. A positive catheter tip by itself is not diagnostic for a CR-BSI; Do not culture the catheter tips routinely, on

removal unless there are clinical signs and symptoms for infection.[7]

Risk factors for AB acquisition in ICU settings have been analyzed in previous reports, but the majority of these studies were performed and found. Male sex, APACHE II score, length of stay in the ICU, mechanical ventilation, prior infection, antimicrobial therapy, and enteral hyperalimentation were associated with *A.baumannii* infection.[19-22] Prior arterial catheterization, thorasic and abdominal drainage do not increase the risk.[14] This study found that immunosuppresion i.e. prior surgery and prior use of antibiotics were related to the development of AB bacteremia. The mortality rate in the ICU among patients who had bacteremia with *A.baumannii* isolates was 100%. Other studies reported crude mortality rate range 27-50%.[10,13] Antibiotic susceptibility testing showed that 85.71% (6/7) were extreme-drug resistant (XDR) i.e. resistant to penicillin, cephalosporine, aminoglycosides, fluoroquinolones as well as carbapenemes. Only sensitive for polymyxins and tegicyclines. Only one strain of *A.baumannii* was sensitive for Imipenem. Jian-nong Wu et al reported in the case of Acinetobacter spp.[11] 50% were for resistance to imipenem. While Vinay Khanna et al found routine antibiotic amikacin and cefoperazone-salbactum were 35.7% each sensitive.[17] Appropriate diagnosis of CLA-BSI based on clinical and microbiological results and antimicrobial resistant patterns of isolated pathogen are very helpful. It also guides the intensivist for specific treatment and patients care.

CONCLUSION

In conclusion, a higher risk of BSI was observed in critically ill patients with respiratory failure, and renal failure cases. Hence, strict control measurements, adequate use of antimicrobial agents, and appropriate use of invasive procedures could be important preventive measures in decreasing the incidence of these infections. The findings of this study may help with implementation of educational and training programs on CLA-BSIs for health care personnel and enable better management of these devices with regard to the prevention, diagnosis and treatment of CLABSIs.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Garcı´a-Garmendia JL, Ortiz-Leyba C. Risk Factors for *Acinetobacter baumannii* Nosocomial Bacteremia in Critically Ill Patients: A Cohort Study. Clinical Infectious Diseases. 2001;33:939-46.
2. Apostolopoulou E. Surviellance of Device associated infection rate and Mortality in 3 greek Intensive are units. Am J crit care. 2013;22(3);e12-e20.
3. Asmita A. Mehta V, Kumar A, Indira K, Suresh G. Nair, Dinesh KR, Singh SK. Risk factors for mortality in Acinetobacter calcoaceticus–baumannii Bacteraemia. Asian Pacific Journal of Tropical Biomedicine. 2012:S1852-S7.
4. Cisneros JM, Rodrı´guez-Ban J. Nosocomial bacteremia due to Acinetobacter baumannii: epidemiology, clinical features and treatment. Clinical Microbiol Infect. 2002;8(11):687-93.
5. Villegas MV, Hartstein AI. Acinetobacter outbreaks, 1977-2000. Infect Control Hosp Epidemiol. 2003;24(4):284-95.
6. 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: A-1-A-20.
7. Ed Septimus. Clinician Guide for Collecting Cultures. CDC. Available on: https://www.cdc.gov/getsmart/healthcare/implementation/clinicianguide.html
8. Manchanda V, Sinha S, Singh NP. Multidrug Resistant Acinetobacter. J Glob Infect Dis. 2010;2(3):291-304.
9. CLSI. Performance standard for Antimicrobial susptibility testing; twenty third informational supplement. M100-S26. 2016;33(1).
10. Kontopoulou K, Tsepanis K, Sgouropoulos I, Triantafyllidou A, Socratous D, Tassioudis P, Chasou E, Antypa E, Renta F, Antoniadou E, Mandraveli K. Risk factors associated with Acinetobacter baumannii septicemia and its mortality rates in critically ill patients. Critical Care. 2013;17(2):P77.
11. Jian-nong Wu, Tie-er Gan, Yue-xian Zhu, Jun-min Cao, Cong-hua Ji, Yi-hua Wu et al. Epidemiology and microbiology of nosocomial bloodstream infections: analysis of 482 cases from a retrospective surveillance study. J Zhejiang Univ Sci B. 2015; 16(1):70-7.
12. Vanitha RN, Kannan G, Venkata N, Vishwakanth D, Nagesh V, Yogitha M et al. A Retrospective study on blood stream infections and antibiotic susceptibility patterns in a tertiary care teaching hospital. Internat J Pharma Pharmaceutl Sci. 2012;4(1):543-48.
13. Wisplinghoff H. Nosocomial Bloodstream Infections in US Hospitals: Analysis of 24,179 Cases from a Prospective Nationwide Surveillance Study.Clin Infect Dis. 2004;39(3):309-17.
14. Zhou HY, Yuan Z, Du YP. Prior use of four invasive procedures increases the risk of Acinetobacter baumannii nosocomial bacteremia among patients in intensive care units: a systematic review and meta-analysis. Int J Infect Dis. 2014; 22:25-30.
15. Soufir L, Timsit JF, Mahe C, Carlet J, Regnier B, Chevret S. Attributable morbidity and mortality of

catheter-related septicemia in critically ill patients: a matched, risk-adjusted, cohort study. Infect Control Hosp Epidemiol. 1999;20:396-401.
16. Apostolopoulou E. Surveillance of Device-Associated Infection rates and mortality in 3 Greek Intensive Care Units. American J Critic Care. 2013;22(3):e12-e20.
17. Khanna V, Mukhopadhayay C, KE V, Verma M, Dabke P. Evaluation of central venous catheter associated blood stream infections: a microbiological observational study. J Pathogens. 2013;1-6.
18. The Joint Commission. Preventing Central Line-Associated Bloodstream Infections: Useful Tools, An International Perspective. Nov 20, 2013. Available on: http://www.jointcommission.org/CLABSIToolkit.
19. Mulin B, Talon D, Viel JF. Risk factors for nosocomial colonization with multiresistant Acinetobacter baumannii. Eur J Clin Microbiol Infect Dis. 1995;14:569-76.
20. Kaul R, Burt JA, Cork L, et al. Investigation of a multiyear multiple critical care unit outbreak due to relatively drug-sensitive Acinetobacter baumannii: risk factors and attributable mortality. J Infect Dis. 1996;174:1279-87.
21. Villers D, Espaze E, Coste-Burel M, et al. Nosocomial Acinetobacter baumannii infections: microbiological and clinical epidemiology. Ann Intern Med. 1998;129:182-9.
22. Seifert H. The Clinical Importance of Microbiological Findings in the Diagnosis and Management of Bloodstream Infections. Clin Infect Dis. 2009;48(Supplement 4):S238-S45.

Cite this article as: Pal N, Sujatha R. Extreme drug resistant *A.baumannii* associated with CLA-BSI in Kanpur. Int J Res Med Sci 2017;5:3620-5.