Infection Prevention in Practice 1 (2019) 100010

Available online at www.sciencedirect.com

Infection Prevention in Practice

journal homepage: www.elsevier.com/locate/ipip

Acinetobacter infections: a retrospective study to determine inhospital mortality rate and clinical factors associated with mortality

R.V. Patel [a], J.S. Shah [a], G. Revathi [b], W. Siika [c], R. Shah [a,*]

[a] Department of Internal Medicine, The Aga Khan University, Nairobi, Kenya
[b] Department of Pathology, The Aga Khan University, Nairobi, Kenya
[c] Department of Critical Care, The Aga Khan University, Nairobi, Kenya

ARTICLE INFO

Article history:
Received 18 April 2019
Accepted 21 June 2019
Available online 28 June 2019

Keywords:
Acinetobacter spp.
Mortality
Clinical factors

SUMMARY

A retrospective case series of acinetobacter infections at a tertiary hospital in Nairobi was conducted to determine the mortality rate and factors associated with mortality. Over an eight-year period, 80 clinically significant infections were identified. The majority of infections were ventilator-associated pneumonia (40%) and bloodstream infections (30%). Eighty-six percent of the isolates were multi-drug resistant. The mortality rate in the study cohort was 45%. Twelve patients grew *Acinetobacter* spp. within 48 h of hospitalization, and three of these patients had no prior healthcare contact. The mean Sequential Organ Failure Assessment score was associated with mortality from acinetobacter infections.

Introduction

Acinetobacter spp. are Gram-negative cocco-bacilli which contribute to a large proportion of hospital-acquired infections in the developing world [1]. They colonize and infect multiple sites, and are frequently multi-drug resistant (MDR). MDR acinetobacter infections result in prolonged hospitalization and may necessitate the use of potentially toxic antimicrobial agents. Risk factors for acinetobacter infections include surgery, invasive lines, mechanical ventilation, enteral feeding and broad-spectrum antibiotic usage [2].

There remains a paucity of data from Africa on acinetobacter infections, with the majority of published data coming from South and West Africa where *Acinetobacter* spp. are among the most common isolates amongst intensive care unit patients. The most common site of infection is the lungs [3]. The mortality rate from acinetobacter infections reported in Africa is between 33% and 60% [4]. Retrospective studies have reported mortality rates ranging between 22.8% and 49.6% in the USA, and between 29% and 71.6% in Europe [5].

Independent predictors of mortality from acinetobacter infections include: chronic obstructive pulmonary disease (COPD), Acute Physiology and Chronic Health Evaluation II score (and other illness severity scores), dialysis, vasopressor use and prior carbapenem administration [6].

* Corresponding author. Department of Internal Medicine, The Aga Khan University, P.O. Box 30270, GPO 00100, Nairobi, Kenya.
E-mail address: reena.shah@aku.edu (R. Shah).

https://doi.org/10.1016/j.infpip.2019.100010

Table I
Demographic and clinical characteristics of the study population.

Variable	Total	Dead (n=36)	Alive (n=44)	P-value
Age in years, mean (SD)	52.6 (17.2)	57.7 (15.9)	48.4 (17.4)	0.015
Sex				
Male (%)	52 (65)	21 (58.3)	31 (70.5)	0.258
Female (%)	28 (35)	15 (41.7)	13 (29.5)	0.258
Length of hospital stay in days, mean (SD)	35.5 (32.5)	29.4 (37.2)	40.5 (27.4)	0.141
Days in hospital before onset of infection, mean (SD)	14.7 (15.5)	13.6 (15.8)	15.6 (15.5)	0.577
SOFA score, mean (SD)	8.07 (5.4)	11.8 (4.5)	4.9 (3.8)	<0.001
Location in hospital				
Critical care (%)	65 (81)	33 (91.7)	32 (72.7)	0.04
Site of infection				
Bloodstream infection (%)	24 (30)	11 (30.6)	13 (29.5)	0.922
Pneumonia (%)	9 (11.25)	3 (8.3)	6 (13.6)	0.455
VAP (%)	32 (40)	18 (50.0)	14 (31.8)	0.099
UTI (%)	2 (2.5)	1 (2.8)	1 (2.3)	0.0886
Skin and soft tissue infection (%)	13 (16.25)	3 (8.3)	10 (22.7)	0.083
Antibiotic usage prior to onset of infection				
Yes (%)	71 (88.75)	34 (94.4)	37 (84.1)	0.145
Antibiotic class used prior to onset of infection				
Cephalosporin (%)	33 (27.27)	11 (30.6)	22 (50.0)	0.079
Quinolone (%)	12 (9.92)	7 (19.4)	5 (11.4)	0.314
Aminoglycoside (%)	13 (10.74)	8 (22.2)	5 (11.4)	0.314
Carbapenem (%)	43 (35.5)	23 (63.9)	20 (45.6)	0.100
Tazobactam-pipericillin (%)	20 (16.53)	8 (22.2)	12 (27.3)	0.604
Presence of invasive lines prior to onset of infection				
Yes (%)	67 (83.75)	34 (94.4)	33 (75.0)	0.019
Site of invasive line(s)				
Central venous catheter (%)	60 (48.78)	34 (27.64)	26 (21.14)	<0.001
Dialysis catheter (%)	31 (25.20)	18 (14.63)	13 (10.57)	0.062
Intra-arterial line (%)	30 (24.39)	10 (8.13)	10 (8.13)	0.604
Intraventricular drain (%)	2 (1.63)	0 (0)	2 (1.63)	0.195
Mechanical ventilation				
Yes (%)	61 (76.25)	31 (86.1)	30 (68.2)	0.061
Mean ventilator-days (SD)	16.3 (17.6)	17.4 (16.4)	15.3 (18.8)	0.597
Comorbid conditions				
DM (%)	32 (42.67)	16 (21.33)	16 (21.33)	0.463
CKD (%)	9 (12)	4 (5.33)	5 (6.67)	0.972
CLD (%)	2 (2.67)	2 (2.67)	0 (0)	0.113
Malignancy (%)	8 (10.67)	6 (8.0)	2 (2.67)	0.072
COPD (%)	7 (9.33)	6 (8.0)	1 (1.33)	0.023

Table I (*continued*)

Variable	Total	Dead (n=36)	Alive (n=44)	P-value
HIV (%)	8 (10.67)	4 (5.33)	4 (5.33)	0.764
CHF (%)	9 (12)	6 (8.0)	3 (4.0)	0.165
Prior use of immunosuppressive medication (including steroids, chemotherapy)				
Yes (%)	24 (30)	14 (38.9)	10 (22.7)	0.119
Surgical procedure during admission				
Yes (%)	42 (52.5)	17 (47.2)	25 (56.8)	0.393
Non-MDR isolates				
Yes (%)	11 (13.75)	3 (8.3)	8 (18.2)	0.203

SOFA, Sequential Organ Failure Assessment; VAP, ventilator-associated pneumonia; UTI, urinary tract infection; DM, diabetes mellitus; CKD, chronic kidney disease; CLD, chronic liver disease; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus; CHF, congestive heart failure; MDR, multi-drug resistant; SD, standard deviation.

Materials and methods

All *Acinetobacter* spp. isolates between 2010 and 2017 were obtained from the laboratory at Aga Khan University Hospital, Nairobi. Blood cultures were performed using BACTEC FX40 Automated Blood Culture System (Becton Dickinson, Franklin Lakes, NJ, USA). Bacterial identification and antibiotic susceptibilities were performed using VITEK 2 Compact, an automated ID/AST Instrument (bioMérieux, Marcy l'Etoile, France). Gram-negative bacilli were tested using the GN 83 AST card which has a panel of 16 antibiotics. The records of patients with isolates of *Acinetobacter* spp. were reviewed to determine if the patient was colonized or infected using pre-determined criteria (Centers for Disease Control and Prevention/National Healthcare Safety Network) for each site of infection [7]. One hundred and twenty-four patients were excluded from the study (16 with missing data, five with polymicrobial specimens and 103 who were colonized), so 80 patients were included in the final analysis. The clinical variables collected were: sex, site of culture, presence of invasive lines, mechanical ventilation, co-morbid conditions, prior use of immunosuppressive medication, location in hospital, prior antimicrobial use, MDR phenotype (resistant to at least one antimicrobial in three different antimicrobial classes [7]), *Acinetobacter* spp. isolated (*A. baumannii*, non-*A. baumannii* isolates), outcome, age, length of hospital stay, duration in hospital prior to first isolate, Sequential Organ Failure Assessment (SOFA) score and mean ventilator-days. Patients who had acinetobacter isolates from multiple sources were counted as one entry.

The data were grouped into two groups (dead vs alive) and analysed for significant differences. Univariate analysis using Chi-squared test and Student's t-test was undertaken to find differences between the two groups. Factors found to be significantly different ($P<0.05$) on univariate analysis were used in multi-variate analysis. Independent associations with mortality were determined based on logistic regression. Survival analysis based on Kaplan–Meier curves coupled with the log rank test was used to demonstrate any differences in survival over time.

Results

Amongst the 204 patients from whom *Acinetobacter* spp. were isolated between 2010 and 2017, 80 had clinically significant infections. Of these, 36 (45%) died. The majority of patients were male (65%), and 65 (81%) were admitted to a critical care unit. The mean age of the study population was 56.3 years, and those who died had a higher mean age (57.7 vs 48.4 years; P=0.015).

Twelve patients grew *Acinetobacter* spp. less than 48 h into their hospital stay. Of these 12 patients, six were transferred from another health facility, three had regular healthcare visits (cancer clinic, renal transplant clinic and dialysis), and three had no documented prior healthcare contact.

The most common site of infection was the lungs [ventilator-associated pneumonia (VAP) 40%], followed by bloodstream infections (BSIs) (30%) and skin and soft tissue infections (16.3%) (Table I). Diabetes was the most common co-morbid condition (42.67%). COPD was more common in those who died (8.0% vs 1.33%; P=0.023). Central venous catheters (CVCs) were the most common invasive devices in both groups (27.64% in those who died, 21.14% in survivors). The mean SOFA score was higher amongst those who died (11.8 vs 4.9; $P\leq0.001$). In total, there were 120 documented antimicrobial drug prescriptions prior to the onset of infection, and carbapenems were prescribed most frequently (35.5%). *A. baumannii* was isolated in 67.5% of cultures. The majority of isolates were MDR on first culture (86.25%).

Based on the univariate analysis, age, critical care admission, SOFA score, presence of a CVC and COPD were found to differ significantly between the two groups. Multi-variate analysis showed independent associations between mortality and SOFA score. The multi-variate analysis was undertaken using continuous values for SOFA score, SOFA score categorized into two groups (0–6 and >6), and SOFA score categorized into two groups (<l3 and >13). The regression model was adjusted for age, COPD and CVC. SOFA score was found to be significantly associated with mortality.

Figure 1 shows the Kaplan–Meier survival curves for variables that differed significantly between the two groups. Based on the log rank tests, differences in CVC, COPD and SOFA score were found to be significant, whereas differences in age (categorized into <50 years and >50 years) were not significant.

Discussion

The mortality rate of 45% found in this study is similar to values reported from outside Africa, but differs from results from Tunisia and South Africa [8]. The study cohort had a

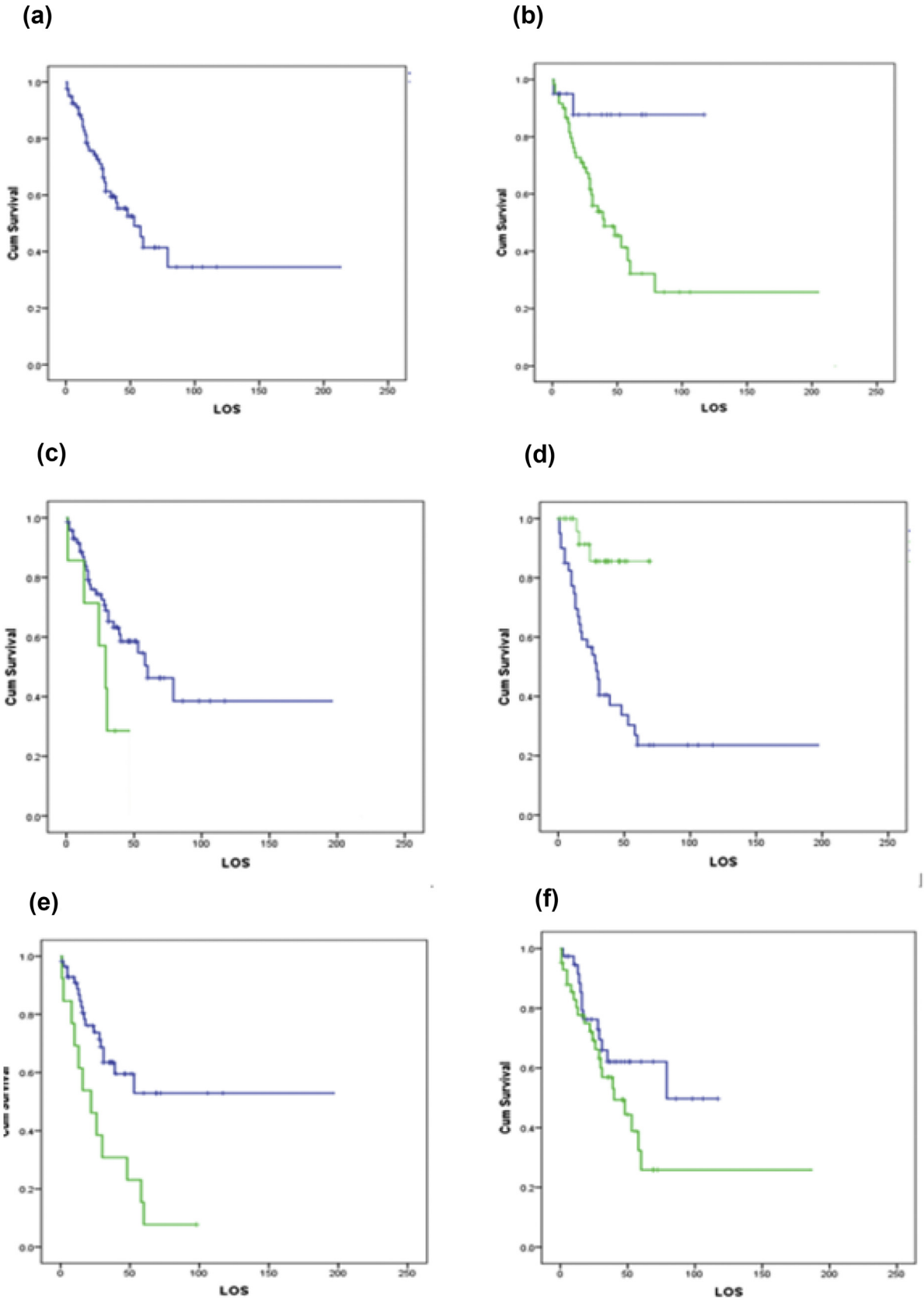

Figure 1. Kaplan–Meier survival curves for (a) overall survival, (b) presence of a central venous catheter (green line, present; blue line, absent), (c) chronic obstructive pulmonary disease (green line, present; blue line, absent), (d) Sequential Organ Failure Assessment (SOFA) score 0–6 (green line, score 0–6; blue line, score >6), (e) SOFA score >13 (green line, score >13; blue line, score <13), and (f) age >50 years (green line, >50 years; blue line <50 years).

younger mean age compared with mean ages found in other studies, and the sex distribution revealed a predominantly male population in this study. Surprisingly, the number of patients with human immunodeficiency virus (HIV) in this study was low given the high prevalence setting. The lung (VAP) was the most common site of infection, which mirrors other studies from Africa, Europe and Asia. There was a high rate of carbapenem usage prior to the onset of acinetobacter infection, but this was not significantly associated with mortality in this study, unlike other studies [4,5]. A study from South Africa found carbapenem and aminoglycoside usage to be significant predictors of mortality (P=0.043 and 0.003, respectively) [4], while other studies found cephalosporin and aminoglycoside usage to be significant predictors ($P\leq$0.001 for both) [9].

This study found that SOFA score was associated with mortality in the patient cohort. Use of the SOFA score as a prediction tool for organ dysfunction and death has undergone extensive research and has been found to be of use in the critical care setting [10]. Significant differences in COPD, age and the presence of an invasive line (CVC) were found between the two survival groups in the present study, but these differences were not significant in multiple regression models. Three patients from this study who had no prior healthcare contact cultured *Acinetobacter* spp. within 48 h of hospitalization, suggesting community acquisition of *Acinetobacter* spp.

In conclusion, to the authors' knowledge, this is the first study to investigate acinetobacter infections in East and Central Africa. Data have been obtained from studies performed in different geographical regions with differing patient populations and characteristics. The mortality rate in the study population reflects that reported in other areas of the world.

The patient cohort had a younger mean age compared with other studies. Surprisingly, the number of patients with HIV was low given the high prevalence setting. There was a high rate of carbapenem use prior to onset of acinetobacter infection, further confirming that widespread unrestricted use of carbapenems can drive antimicrobial resistance and select for bacteria such as *Acinetobacter* spp. It is hoped that infection rates will reduce with good antimicrobial stewardship, which has been initiated at the study institution.

The SOFA score was found to be a good predictor of mortality in the patient cohort. COPD, age and the presence of an invasive line (CVC) differed significantly between the two groups, but these differences were not significant in multiple regression models.

Acinetobacter infections are an emerging cause of hospital-acquired infections globally. The importance of vigilance in surveillance, early detection and prompt treatment are highlighted to prevent significant mortality among affected patients. Further research will need to be undertaken to determine the best therapeutic options in the local setting.

Conflict of interest statement

None declared.

Funding source

None.

Acknowledgements

The authors wish to thank the Research and Medical Records Department at Aga Khan University Hospital, Nairobi for their guidance and support.

References

[1] Peleg AY, Seifert H, Paterson DL. *Acinetobacter baumannii*: emergence of a successful pathogen. Clin Microbiol Rev 2008;21:538—82.
[2] Kempf M, Rolain JM. Emergence of resistance to carbapenems in *Acinetobacter baumannii* in Europe: clinical impact and therapeutic options. Int J Antimicrob Agents 2012;39:105—14.
[3] Munoz-Price LS, Weinstein RA. Acinetobacter infection. N Engl J Med 2008;358:1271—81.
[4] Ntusi NBA, Badri M, Khalfey H, Whitelaw A, Oliver S, Piercy J, et al. ICU-associated *Acinetobacter baumannii* colonisation/infection in a high HIV-prevalence resource-poor setting. PLoS One 2012;7:1—7.
[5] Ramanathan S, Suda KJ, Fitzpatrick MA, Poggensee L, LaVela SL, Burns SP, et al. Multidrug-resistant acinetobacter: risk factors and outcomes in veterans with spinal cord injuries and disorders. Am J Infect Control 2017;45:1183—9.
[6] Djordjevic ZM, Folic MM, Folic ND, Gajovic N, Gajovic O, Jankovic SM. Risk factors for hospital infections caused by carbapanem-resistant *Acinetobacter baumannii*. J Infect Dev Ctries 2016;10:1073—80.
[7] Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315:801.
[8] Chaari A, Mnif B, Bahloul M, Mahjoubi F, Chtara K, Turki O, et al. *Acinetobacter baumannii* ventilator-associated pneumonia: epidemiology, clinical characteristics, and prognosis factors. Int J Infect Dis 2013;17:e1225—8.
[9] Villar M, Cano ME, Gato E, Garnacho-Montero J, Miguel Cisneros J, Ruíz de Alegría C, et al. Epidemiologic and clinical impact of *Acinetobacter baumannii* colonization and infection. Medicine (Balt) 2014;93:202—10.
[10] Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. Intensive Care Med 1996;22:707—10.