July 2019

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Rajiv Patel
Aga Khan University

Jasmit Shah
Aga Khan University, jasmit.shah@aku.edu

Gunturu Revathi
Aga Khan University, gunturu.revathi@aku.edu

Wangari Siika
Aga Khan University, wangari.siika@aku.edu

Reena Shah
Aga Khan University, reena.shah@aku.edu

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Recommended Citation
Patel, R., Shah, J., Revathi, G., Siika, W., Shah, R. (2019). Acinetobacter infections: a retrospective study to determine in hospital mortality rate and clinical factors associated with mortality. Infection Prevention in Practice, 1.
Available at: https://ecommons.aku.edu/eastafrica_fhs_mc_intern_med/108
Acinetobacter infections: a retrospective study to determine in-hospital 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

A R T I C L E   I N F O
Article history:
Received 18 April 2019
Accepted 21 June 2019
Available online 28 June 2019

Keywords:
Acinetobacter spp.
Mortality
Clinical factors

S U M M A R Y
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.© 2019 The Authors. Published by Elsevier Ltd on behalf of The Healthcare Infection Society. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Acinetobacter spp. are Gram-negative coco-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
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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) | 24 (30)   | 14 (38.9)   | 10 (22.7)    | 0.119   |
| Surgical procedure during admission                                      | Yes (%)   | 42 (52.5)   | 17 (47.2)    | 0.393   |
| Non-MDR isolates                                                         | Yes (%)   | 11 (13.75)  | 3 (8.3)      | 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<0.001). 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 (<13 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 ($P<0.001$ 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 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.

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