Original Research Article

SAGE Open Medicine

SAGE Open Medicine
Volume 9: 1–5

DOI: 10.1177/20503121211001144
journals.sagepub.com/home/smo
SAGE

Prevalence of multidrug-resistant *Acinetobacter baumannii* in a critical care setting: A tertiary teaching hospital experience

Thabit Alotaibi, Abdulrhman Abuhaimed, Mohammed Alshahrani, Ahmed Albdelhady, Yousef Almubarak and Osama Almasari

Abstract

Background: The management of *Acinetobacter baumannii* infection is considered a challenge especially in an intensive care setting. The resistance rate makes it difficult to manage and is believed to lead to higher mortality. We aim to investigate the prevalence of *Acinetobacter baumannii* and explore how different antibiotic regimens could impact patient outcomes as there are no available published data to reflect our population in our region.

Methods: We conducted a retrospective review of all infected adult patients admitted to the intensive care unit at King Fahad University Hospital with a confirmed laboratory diagnosis of *Acinetobacter baumannii* from 1 January 2013 until 31 December 2017. Positive cultures were obtained from the microbiology department and those meeting the inclusive criteria were selected. Variables were analyzed using descriptive analysis and cross-tabulation. Results were further reviewed and audited by blinded co-authors.

Results: A comprehensive review of data identified 198 patients with *Acinetobacter baumannii*. The prevalence of *Acinetobacter baumannii* is 3.37%, and the overall mortality rate is 40.81%. Our sample consisted mainly of male patients, that is, 68.7%, with a mean age of 49 years, and the mean age of female patients was 56 years. The mean age of survivors was less than that of non-survivors, that is, 44.95 years of age. We observed that prior antibiotic use was higher in non-survivors compared to survivors. From the review of treatment provided for patients infected with *Acinetobacter baumannii*, 65 were treated with colistin alone, 18 were treated with carbapenems, and 22 were treated with a combination of both carbapenems and colistin. The mean length of stay of *Acinetobacter baumannii*–infected patients was 20.25 days. We found that the survival rates among patients who received carbapenems were higher compared to those who received colistin.

Conclusion: We believe that multidrug-resistant *Acinetobacter baumannii* is prevalent and associated with a higher mortality rate and represents a challenging case for every intensive care unit physician. Further prospective studies are needed.

Keywords

Intensive care, infection, Acinetobacter Baumannii, *A.* baumannii, sepsis, pneumonia

Date received: 15 February 2021; accepted: 15 February 2021

Background

Multidrug-resistant (MDR) organism, though no uniform definition exists, is defined as the isolate resistant to at least three different classes of antimicrobial agents in vitro.[1] Infections caused by MDR *Acinetobacter* spp. have always been difficult for physicians and microbiologists to manage. It possesses characteristics that allow it to maintain its survival for an extended period on surfaces, resulting in it being a common cause for healthcare-associated infections[2,3] that include bacteremia, pneumonia, urinary tract infection, wound infections, and meningitis.

Imam Abdulrahman bin Faisal University, Dammam, Saudi Arabia

Corresponding author:
Thabit Alotaibi, Imam Abdulrahman bin Faisal University, Dammam 34221, Saudi Arabia.
Email: Alotaibi.thabit@gmail.com

Hospitalized patients in non-intensive care settings were also at risk of being carriers of the organism with rates as high as 75% on the skin.[4] High colonization was also observed in intensive care unit (ICU) patients, especially on their respiratory tract. Treatment of *Acinetobacter baumannii*–related infections is highly reliant on appropriate empirical antimicrobial therapy, which is critical for survival in severe cases. The usual path of treatment starts with carbapenems as the drug of choice. They are the first-line agents in highly susceptible organisms. Unfortunately, *A. baumannii* is a very elusive organism with a remarkable capacity for developing resistance. This resulted in the development of carbapenem-resistant *A. baumannii* (CRAB). Currently, polymyxins are the antimicrobial agents with the highest level of in vitro performance against *A. baumannii*; however, reports of its resistance have been documented.[5]

The development of resistance to *A. baumannii* can be attributed to several mechanisms: inactivation of β-lactams by β-lactamases (classes A, B, C, D) and resistance through efflux pump, which can lead to resistance to carbapenems and the formation of biofilms with sub-inhibitory concentrations of antibiotics. A change in membrane permeability is another mechanism as well as modification of antibiotic target site with other known methods that are studied on how *A. baumannii* becomes resistant.[6] Class A β-lactamases hydrolyze penicillins and cephalosporins. They include narrow-spectrum and extended-spectrum β-lactamases, with SHV-5 being one of them. Class B β-lactamases strongly hydrolyze β-lactams, and metal chelators like EDTA are considered inhibitors. Class C β-lactamases are resistant to extended-spectrum cephalosporins due to intrinsic encoding of AmpC cephalosporinases. Class D β-lactamases, also called oxacillinases, are serine-dependent like class A, class C, and class D.[7]

Many case–control studies reported prior exposure to carbapenems and third-generation cephalosporins to be the commonest risk factor, followed by fluoroquinolones, aminoglycosides, and metronidazole. Being mechanically ventilated is the second most common risk factor.[5] Current ICU admission, length of stay (LOS), severity of illness, recent surgery, and invasive procedures are considered risk factors.[8–12] Prior colonization with CRAB is another independent risk factor that has been observed. A direct correlation has been reported between colonization pressure and acquiring the pathogen.[13] The use of colistin and/or rifampin was shown to be an effective treatment option, and another study in Baltimore revealed that LOS is associated with mortality rate in case of methicillin-resistant *Staphylococcus aureus* (MDRA) independently.[14–19]

Our objective was to investigate the prevalence of infections caused by *A. baumannii* in a local general medical ICU (MICU) and surgical ICU (SICU) of a tertiary teaching hospital, to identify the risk factors associated with this kind of infections, and to study the outcome of the affected patients in terms of survivability and LOS.

Methods

Study design and setting

This is a retrospective cohort study that included all adult patients infected with *A. baumannii* who were admitted to the ICU at King Fahad Hospital of the University, Khobar, Saudi Arabia, from 1 January 2014 to 31 December 2017. Ethical approval was waived from the Institutional Review Board (IRB) office at the establishment.

The ICU consists of 12 beds of MICU and 11 beds of SICU, with each having a multidisciplinary team of ICU physicians, respiratory therapists, nursing team, clinical pharmacists, clinical dietitians, and infectious disease specialists. The annual admission rate is about 900 per year with a bed occupancy of 91.75%.

Patient selection and case definition

MDR *A. baumannii* will be defined as the isolate resistant to at least three classes of antimicrobial agents—all penicillins and cephalosporins (including inhibitor combinations), fluoroquinolones, and aminoglycosides. All infected adult patients above the age of 18 years were admitted to the ICU during the study period with a confirmed positive culture of MDR *A. baumannii* during their current admission. All patients with previous positive cultures before their admission to the ICU and all patients with screening cultures were excluded. The infectious disease specialists and the microbiology department were involved in the process of patient selection and enrollment for the study.

Data collection

Data were collected retrospectively through multiple stages; it initially started with a full list of all positive MDR cultures from the microbiology department, and then we went through the list and identified cases that met the inclusion criteria. We ensured that an extensive file review of each case was done using both digital base and paper base data and filled out the variable data collection sheet over a 6-month period. The final data were further reviewed and audited by blinded personnel.

Statistical analysis

We cross-referenced all collected data, and a random selection of cases was done. We audited and confirmed the absence of duplication or missed data. The statistical analysis of collected audited data was done using IBM SPSS software v.25. Multiple methods for analysis were used, including cross-tabulation, descriptive analysis, and statistical hypothesis testing depending on the present variables.

Results

From 1 January 2013 until 31 December 2017, we had a total of 5864 admissions to our ICU. For those with a diagnosis of *A.*

Table 1. Baseline characteristics.

		Non-survivors (N = 80)	Survivors (N = 118)
Age (SD)		61.1 (±22.01)	44.95 (±21.36)
Gender	Female	26	36
	Male	54	82
Hypertension		38	34
Diabetes		41	33
Mechanically ventilated		62	73
Prior antibiotic use[a]		22	10

SD: standard deviation.
[a]Prior antibiotic use.
[b]Combined colistin and carbapenems.

baumannii, a total of 198 patients were identified with confirmed laboratory cultures of *A. baumannii*. The prevalence of *A. baumannii* is 3.37%, and the overall mortality rate is 40.81%.

Our sample consists mainly of male patients of 68.7% and female patients of 31.3%. The mean age of males is 49 years and of females is 56 years.

Table 1 shows the baseline characteristics. We divided our cohort into survivors and non-survivors. The mean age of survivors is less than that of non-survivors, that is, 44.95 years of age. In terms of comorbidities, 38 non-survivors had hypertension, while 41 out of 80 had diabetes. Prior empirical antibiotic use was observed in 22 non-survivors. In terms of antibiotic coverage, colistin was given to 65 patients. Carbapenems were given to 18 patients, and the combination of colistin and carbapenems was given to 22 patients. Other characteristics are shown in Table 1.

The working diagnoses leading to ICU admissions mainly were community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), and urinary tract infections (UTIs). We compared the LOS of *A. baumannii*–infected patients to our general ICU mean LOS during the study period. We found that the mean LOS of *A. baumannii* is 20.25 days compared to 21.8 days of our ICU mean LOS.

We looked at how colistin and/or carbapenems affect the survivability of patients in Table 2. We found that of the 65 patients taking colistin, 45% survived, while of the 18 patients taking carbapenems, 72% survived.

Table 2. Survival rates of subjects on different types of antibiotic regimens.

	How many patients	Non-survivors	Survivors
Colistin	65	36 (55%)	29 (45%)
Carbapenems	18	5 (28%)	13 (72%)
Combined	22	13 (59%)	9 (41%)
Others	93	26 (28%)	67 (72%)

Discussion

The resistance of *Acinetobacter* species to antimicrobial agents caused a challenge to healthcare providers especially with the use of broad-spectrum antibiotic agents and transmission among patients.[20]

A report from five European countries showed various resistance of *Acinetobacter* spp. to various agents, including imipenem, ceftazidime, amikacin, and others[21]

The MYSTIC (Meropenem Yearly Susceptibility Test Information Collection) program reported that imipenem and meropenem were found as the most active agents against *A. baumannii*, with resistance rates of 16% and 18%, respectively. Subsequent data from the MYSTIC program (2006) revealed a substantial increase in resistance rates for meropenem (43.4%) and imipenem (42.5%).[22,23]

In our study, the prevalence of 3.37% is considered lower when compared with a report from 2010.[24] However, up to our knowledge, there are no data available on the prevalence of *A. baumannii* MDR in the eastern region of the kingdom or other regions as reported by Yaseen M Arabi in his publication in 2019.[25]

Looking at the risk factors, a retrospective study of 247 patients by Dent et al.[26] showed that mechanical ventilation and previous drug use are important risk factors and showed increased mortality rates. In our study, 68.1% were mechanically ventilated before developing MDR and 32.8% had prior use of colistin. This goes with what is in the literature about the known risk factors of *A. baumannii*, with mortality due to being mechanically ventilated and prior colistin use being 77.5% and 45%, respectively. An observational study reported that *A. baumannii* is the third most common pathogen associated with ventilator-associated pneumonia (VAP).[27]

Looking into our data, it is shown that local practice for treatment, guided by culture results, showed that the use of colistin, carbapenems, or the combination of both leads to a higher rate of survival of 72% compared to colistin, and the same rate if carbapenems were given. This could be due to the high rate of resistance of *A. baumannii*, where the literature also suggests the use of colistin as part of empirical coverage in ICU.[28]

Internationally, novel antimicrobial agents are being investigated as a potential treatment for highly resistant organisms. Isler et al. mention cefiderocol (siderophore cephalosporin) as the first of new agents against CRAB to be approved for clinical use. Its definitive effectiveness is to be observed and tested in phase III trials currently ongoing. Eravacycline (tetracyclines) is another potential emerging agent showing better in vitro activity than tigecycline; however, phase III trials are still to be done for this possible agent.[29] To the best of our knowledge and after contacting local authorities, these agents are yet to be available in our region.

This study carries some limitations as the retrospective nature of it cannot eliminate the risk of selection bias and did not allow to make a better correlation between timing, type, and duration of empirical antimicrobial therapy as reported risk factors and the exact correlation between resistance and clinical outcomes. For the same reason, we could not verify

the exact mechanism of resistance of *A. baumannii*. However, as future quality improvement projects in the unit, these variables were incorporated into the prospectively collected ICU database. This initiative laid the groundwork for multiple prospective projects that we will investigate, in detail, the resistance pattern of MDR *A. baumannii* in our region and its response to the current standard of care. Also, since the nature of the study is retrospective, we included all the participants as per the inclusion criteria and we did not include in our analysis the sample size/power for this study.

Conclusion

MDR *A. baumannii* is prevalent and can be associated with higher mortality. The lack of specific microbiological data makes it challenging for critical care and infectious disease physicians to manage. Further prospective studies are needed to thoroughly investigate and treat *A. baumannii* infections.

Acknowledgements

We appreciate the contributions of our Critical Care staff including training residents, nursing staff, microbiology laboratory personnel, and infection control personnel. We also like to extend our thanks and appreciation to our research assistant office for their hard work and support for this project. This project was not funded by any institution, and all authors contributed to this project on their own time. I would like to especially thank our research coordinator Charlene for her efforts.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Ethical approval was waived from the IRB office of Imam Abdulrahman bin Faisal University—Research and Higher Studies (IRB Number: N2015104).

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Informed consent

Informed consent was waived due to the nature of this study being retrospective, and the data collection process made sure to protect all patient personal data.

Trial registration

This study was not registered as it is not a prospective/RCT study

ORCID iDs

Thabit Alotaibi https://orcid.org/0000-0002-5757-2814

Abdulrhman Abuhaimed https://orcid.org/0000-0002-0915-9910

Mohammed Alshahrani https://orcid.org/0000-0001-6814-0075

References

1. Magiorakos AP, Srinivasan A, Carey RB, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect* 2012; 18(3): 268–281.
2. Fournier PE and Richet H. The epidemiology and control of Acinetobacter baumannii in health care facilities. *Clin Infect Dis* 2006; 42: 692–699.
3. Jawad A, Heritage J, Snelling AM, et al. Influence of relative humidity and suspending menstrua on survival of Acinetobacter spp. *J Clin Microbiol* 1996; 34(12): 2881–2887.
4. Seifert H, Dijkshoorn L, Gerner-Smidt P, et al. Distribution of Acinetobacter species on human skin: comparison of phenotypic and genotypic identification methods. *J Clin Microbiol* 1997; 35(11): 2819–2825.
5. Gales AC, Jones RN and Sader HS. Contemporary activity of colistin and polymyxin B against a worldwide collection of Gram-negative pathogens: results from the SENTRY Antimicrobial Surveillance Program (2006-09). *J Antimicrob Chemother* 2011; 66(9): 2070–2074.
6. Lee CR, Lee JH, Park M, et al. Biology of Acinetobacter baumannii: pathogenesis, antibiotic resistance mechanisms, and prospective treatment options. *Front Cell Infect Microbiol* 2017; 7: 55.
7. Ayoub Moubareck C and Hammoudi Halat D. Insights into Acinetobacter baumannii: A review of microbiological, virulence, and resistance traits in a threatening nosocomial pathogen. *Antibiotics* 2020; 9: 119.
8. Falagas ME and Kopterides P. Risk factors for the isolation of multi-drug-resistant Acinetobacter baumannii and Pseudomonas aeruginosa: a systematic review of the literature. *J Hosp Infect* 2006; 64: 7–15.
9. Landman D, Quale JM, Mayorga D, et al. Citywide clonal outbreak of multiresistant Acinetobacter baumannii and Pseudomonas aeruginosa in Brooklyn, NY: the preantibiotic era has returned. *Arch Intern Med* 2002; 162: 1515–1520.
10. Cisneros JM, Rodríguez Baño J, Fernández Cuenca F, et al. Risk-factors for the acquisition of imipenem-resistant Acinetobacter baumannii in Spain: a nationwide study. *Clin Microbiol Infect* 2005; 11: 874–879.
11. Medina J, Formento C, Pontet J, et al. Prospective study of risk factors for ventilator-associated pneumonia caused by Acinetobacter species. *J Crit Care* 2007; 22: 18–27.
12. Katsaragakis S, Markogiannakis H, Toutouzas KG, et al. Acinetobacter baumannii infections in a surgical intensive care unit: predictors of multidrug resistance. *World J Surg* 2008; 32: 1194–1202.
13. D'Agata EM, Thayer V and Schaffner W. An outbreak of Acinetobacter baumannii: the importance of cross-transmission. *Infect Control Hosp Epidemiol* 2000; 21(9): 588–591.
14. Bassetti M, Repetto E, Righi E, et al. Colistin and rifampicin in the treatment of multidrug-resistant Acinetobacter baumannii infections. *J Antimicrob Chemother* 2008; 61(2): 417–420.
15. Li J, Rayner CR, Nation RL, et al. Heteroresistance to colistin in multidrug-resistant Acinetobacter baumannii. *Antimicrob Agents Chemother* 2006; 50(9): 2946–2950.
16. Garnacho-Montero J, Ortiz-Leyba C, Jiménez-Jiménez FJ, et al. Treatment of multidrug-resistant Acinetobacter baumannii ventilator-associated pneumonia (VAP) with intravenous

colistin: a comparison with imipenem-susceptible VAP. *Clin Infect Dis* 2003; 36(9): 1111–1118.
17. Kallel H1, Hergafi L, Bahloul M, et al. Safety and efficacy of colistin compared with imipenem in the treatment of ventilator-associated pneumonia: a matched case-control study. *Intensive Care Med* 2007; 33(7): 1162–1167.
18. Betrosian AP1, Frantzeskaki F, Xanthaki A, et al. Efficacy and safety of high-dose ampicillin/sulbactam vs. colistin as monotherapy for the treatment of multidrug resistant Acinetobacter baumannii ventilator-associated pneumonia. *J Infect* 2008; 56(6): 432–436.
19. Sunenshine RH, Wright M-O, Maragakis LL, et al. Multidrug-resistant *Acinetobacter* infection mortality rate and length of hospitalization. *Emerg Infect Dis* 2007; 13(1): 97–103.
20. Maragakis LL and Perl TM. Acinetobacter baumannii: epidemiology, antimicrobial resistance, and treatment options. *Clin Infect Dis* 2008; 46: 1254–1263.
21. Hanberger H, Garcia Rodriguez JA, Gobernado M, et al. Antibiotic susceptibility among aerobic gram-negative bacilli in intensive care units in 5 European countries. French and Portuguese ICU Study Groups. *JAMA* 1999; 281: 67–71.
22. Turner PJ and Greenhalgh JM and MYSTIC Study Group (Europe). The activity of meropenem and comparators against Acinetobacter strains isolated from European hospitals, 1997-2000. *Clin Microbiol Infect* 2003; 9: 563–567.
23. Turner PJ. Meropenem activity against European isolates: report on the MYSTIC (Meropenem Yearly Susceptibility Test Information Collection) 2006 results. *Diagn Microbiol Infect Dis* 2008; 60(2): 185–192.
24. Saeed NK, Kambal AM and El-Khizzi NA. Antimicrobial-resistant bacteria in a general intensive care unit in Saudi Arabia. *Saudi Med J* 2010; 31(12): 1341–1349.
25. Kharaba A, Abdelaziz Hussein MA, Al-Hameed FM, et al. Acinetobacter baumannii in Saudi Arabia: the new growing threat. *Saudi Crit Care J* 2019; 3: 54–57.
26. Dent LL, Marshall DR, Pratap S, et al. Multidrug resistant Acinetobacter baumannii: a descriptive study in a city hospital. *BMC Infect Dis* 2010; 10: 196.
27. Koulenti D, Lisboa T, Brun-Buisson C, et al. Spectrum of practice in the diagnosis of nosocomial pneumonia in patients requiring mechanical ventilation in European intensive care units. *Crit Care Med* 2009; 37(8): 2360–2368.
28. Garnacho-Montero J, Dimopoulos G, Poulakou G, et al. Task force on management and prevention of Acinetobacter baumannii infections in the ICU. *Intensive Care Med* 2015; 41(12): 2057–2075.
29. Isler B, Doi Y, Bonomo RA, et al. New treatment options against carbapenem-resistant Acinetobacter baumannii infections. *Antimicrob Agents Chemother* 2019; 63(1): e01110-18.