First case of NDM-1-producing Acinetobacter baumannii isolated in Timor-Leste

Nevio Sarmento, Tessa Oakley, Joana C Belo, Virginia L da Conceição, Carolina da C Maia, Celia G Santos, Elfiana Amaral, Lucia Toto, Endang S da Silva, Ian Marr, Jennifer Yan, Joshua R Francis

Carbapenem antibiotics are important in the treatment of infections caused by bacteria in the order Enterobacterales which are resistant to multiple classes of antibiotics. Due to their high levels of intrinsic resistance, strains of Acinetobacter baumannii complex organisms resistant to carbapenems pose an important public health issue.1,2 Carbapenem-resistant A. baumannii (CRAB) is mainly due to acquisition of carbapenem-hydrolysing oxacillinase-encoding class D (OXA) genes which can be either plasmid- or chromosomally-encoded or through modification on the outer membrane protein and efflux pump.3 Although class B metallo-β-lactamases (MBLs) are not the most common mechanism of resistance seen in CRAB isolates, MBL-positive A. baumannii are increasingly reported worldwide.1 While this resistance mechanism was first described in an isolate of K. pneumoniae in 2008, many countries have since isolated strains of New Delhi metallo-beta-lactamase 1 (NDM-1) -carrying A. baumannii .4 We describe the first of these strains isolated in Timor-Leste.

At the main referral hospital in Dili (Hospital Nacional Guido Valadares), the capital city of Timor-Leste, a high rate of infections caused by extended spectrum beta lactamase (ESBL) - producing organisms has resulted in frequent use of meropenem as a treatment for bacteraemia and other invasive infections. 5

In December 2020, an Acinetobacter baumannii complex organism was identified in a urine sample culture from a 39-year-old male admitted to hospital in Dili. The patient had no previous healthcare contact or movement outside of Timor-Leste. The organism was identified by matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI-TOF/MS) (Bruker Daltonik, Bremen, Germany) and automated antimicrobial susceptibility testing (AST) performed on BD Phoenix M50 (Becton Dickinson, Berks, United Kingdom). The AST interpretations were performed as per European Committee on Antimicrobial Susceptibility Testing (EUCAST) and the organism was found to be resistant to almost all antibiotics including meropenem (minimum inhibitory concentration, MIC ≥ 8 µg/L), trimethoprim/sulfamethoxazole (MIC ≥ 4/76 µg/L), and gentamicin (MIC ≥ 4 µg/L). The only antibiotic to which the isolate was found to be susceptible was amikacin (MIC = 8 µg/L; Table 1). This organism was identified as a class B carbapenemase by BD Phoenix NMIC-502 panel and subsequent molecular testing utilising Xpert® Carba-R (Cepheid, Sunnyvale, USA) confirmed the isolate as an NDM-1 producer.

Recommended treatment options for clinically significant isolates of carbapenem-resistant A. baumannii may include minocycline, ampicillin-sulbactam and colistin, and are currently unavailable in Timor-Leste. Meropenem is on the Timor-Leste Essential Medicines List and is usually available. The Essential Medicines List does not currently include amikacin, piperacillin-tazobactam, or any fourth-generation cephalosporin.

This is the first report of an NDM-1-producing multidrug-resistant A. baumannii from Timor-Leste. The discovery of this extensively-drug resistant strain is worrying, especially as infections caused by A. baumannii complex are often related to prolonged hospitalisation and to death. 6 The identification of an NDM-1-carrying strain in a clinical isolate in Timor-Leste highlights the need for ongoing clinical and laboratory surveillance, and established infection control protocols to limit spread in the national and referral hospitals.

Table 1: MIC values of the *A. baumannii* isolate

|  |  |  |
| --- | --- | --- |
| Antibiotic | MIC (µg/mL) | Interpretationa |
| Amikacin | 8 | S |
| Amoxicillin-clavulanate (f) | > 32/2 | R |
| Ampicillin | > 8 | R |
| Aztreonam | > 16 | R |
| Ceftriaxone | > 4 | R |
| Cefuroxime | > 8 | R |
| Cephalexin | > 16 | R |
| Ciprofloxacin | > 1 | R |
| Ertapenem | > 1 | R |
| Fosfomycin | 128 | R |
| Gentamicin | > 4 | R |
| Imipenem | > 8 | R |
| Levofloxacin | > 2 | R |
| Meropenem | > 8 | R |
| Nitrofurantoin | > 64 | R |
| Tobramycin | > 4 | R |
| Trimethoprim-sulfamethoxazole | > 4/76 | R |

a R: resistant; S: susceptible.

# Funding

This work was made possible through the support of the Fleming Fund Country Grant for Timor-Leste (FF/17/233), which has facilitated significant improvements in laboratory capacity for diagnosis and surveillance of antimicrobial resistance in Timor-Leste. The Fleming Fund is a UK aid investment programme to tackle antimicrobial resistance in low- and middle-income countries around the world and is managed by the UK Department of Health and Social Care.

# Declaration of competing interest

None declared.

# Ethical approval

Not required.

# Author details

Nevio Sarmento 1

Tessa Oakley 1

Joana C Belo 1

Virginia L da Conceição 1

Carolina da C Maia 2

Celia G Santos 3

Elfiana Amaral 1

Lucia Toto 1

Endang S da Silva 2

Ian Marr 4

Jennifer Yan 1,5

Joshua R Francis 1,5

1. Menzies School of Health Research, Dili, Timor-Leste.
2. Laboratório Nacional de Saúde, Dili, Timor-Leste
3. Departamento Medicina Interna, Hospital Nacional Guido Valadares, Dili, Timor-Leste
4. The Canberra Hospital, ACT, Australia
5. Royal Darwin Hospital, NT, Australia

## Corresponding author

Nevio Sarmento

Menzies School of Health Research, Dili, Timor-Leste

email: nevio.sarmento@menzies.edu.au

# References

1. Wang J, Ning Y, Li S, Mang Y, Liang J, Jin C et al. Multidrug-resistant Acinetobacter baumannii strains with NDM-1: molecular characterization and in vitro efficacy of meropenem-based combinations. Exp Ther Med . 2019;18(4):2924–32. doi: https://doi.org/10.3892/etm.2019.7927.
2. Govind CN, Moodley K, Peer AK, Pillay N, Maske C, Wallis C et al. NDM-1 imported from India - first reported case in South Africa. S Afr Med J . 2013;103(7):476–8. doi: https://doi.org/10.7196/samj.6593.
3. Hamidian M, Nigro SJ. Emergence, molecular mechanisms and global spread of carbapenem-resistant Acinetobacter baumannii . Microb Genom . 2019;5(10):e000306. doi: https://doi.org/10.1099/mgen.0.000306.
4. Yong D, Toleman MA, Giske CG, Cho HS, Sundman K, Lee K et al. Characterization of a new metallo-β-lactamase gene, bla NDM-1 , and a novel erythromycin esterase gene carried on a unique genetic structure in Klebsiella pneumoniae sequence type 14 from India. Antimicrob Agents Chemother . 2009;53(12):5046–54. doi: https://doi.org/10.1128/AAC.00774-09.
5. Marr I, Sarmento N, O’Brien M, Kee L, Gusmao C, de Castro G et al. Antimicrobial resistance in urine and skin isolates in Timor-Leste. J Glob Antimicrob Resist . 2018;13:135–8. doi: https://doi.org/10.1016/j.jgar.2017.12.010.
6. Shu H, Li L, Wang Y, Guo Y, Wang C, Yang C et al. Prediction of the risk of hospital deaths in patients with hospital-acquired pneumonia caused by multidrug-resistant Acinetobacter baumannii Infection: a multi-center study. Infect Drug Resist . 2020;13:4147–54. doi: https://doi.org/10.2147/IDR.S265195.

**Communicable Diseases Intelligence**

ISSN: 2209-6051 Online

**Communicable Diseases Intelligence (CDI) is a peer-reviewed scientific journal published by the Office of Health Protection and Response, Department of Health and Aged Care. The journal aims to disseminate information on the epidemiology, surveillance, prevention and control of communicable diseases of relevance to Australia.**

**Editor:** Noel Lally

**Deputy Editor:** Simon Petrie

**Design and Production:** Kasra Yousefi

**Editorial Advisory Board:** David Durrheim, Mark Ferson, John Kaldor, Martyn Kirk and Linda Selvey

**Website**: <http://www.health.gov.au/cdi>

**Contacts**CDI is produced by the Office of Health Protection and Response, Australian Government Department of Health and Aged Care, GPO Box 9848, (MDP 6) CANBERRA ACT 2601

**Email:** [cdi.editor@health.gov.au](mailto:cdi.editor@health.gov.au)

**Submit an Article**You are invited to submit your next communicable disease related article to the Communicable Diseases Intelligence (CDI) for consideration. More information regarding CDI can be found at: <http://health.gov.au/cdi>.

Further enquiries should be directed to: [cdi.editor@health.gov.au](mailto:cdi.editor@health.gov.au).

This journal is indexed by Index Medicus and Medline.

Creative Commons Licence - Attribution-NonCommercial-NoDerivatives CC BY-NC-ND

© 2022 Commonwealth of Australia as represented by the Department of Health and Aged Care

This publication is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International Licence from <https://creativecommons.org/licenses/by-nc-nd/4.0/legalcode> (Licence). You must read and understand the Licence before using any material from this publication.

**Restrictions**The Licence does not cover, and there is no permission given for, use of any of the following material found in this publication (if any):

* the Commonwealth Coat of Arms (by way of information, the terms under which the Coat of Arms may be used can be found at [www.itsanhonour.gov.au](http://www.itsanhonour.gov.au/));
* any logos (including the Department of Health and Aged Care’s logo) and trademarks;
* any photographs and images;
* any signatures; and
* any material belonging to third parties.

**Disclaimer**Opinions expressed in Communicable Diseases Intelligence are those of the authors and not necessarily those of the Australian Government Department of Health and Aged Care or the Communicable Diseases Network Australia. Data may be subject to revision.

**Enquiries**Enquiries regarding any other use of this publication should be addressed to the Communication Branch, Department of Health and Aged Care, GPO Box 9848, Canberra ACT 2601, or via e-mail to: [copyright@health.gov.au](mailto:copyright@health.gov.au)

**Communicable Diseases Network Australia**Communicable Diseases Intelligence contributes to the work of the Communicable Diseases Network Australia.  
<http://www.health.gov.au/cdna>