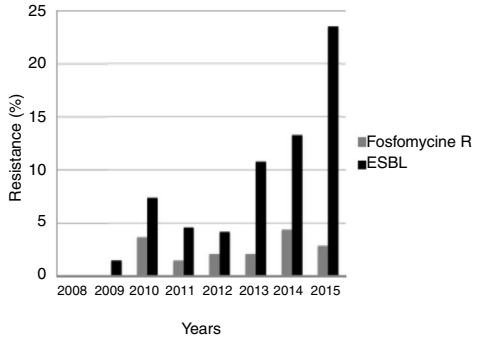

Fig. 1. Trends in fosfomycin resistance and ESBL production in *E. coli* isolated from males with febrile urinary tract infection over the study period.
Abbreviations: R: resistant; ESBL: extended-spectrum beta-lactamase.

and less frequently to plasmid modifying enzymes, mainly the *fosA3*.[4] The *fosA3* genes, commonly located on a conjugative plasmid that also carries a CTX-M, are widespread in East Asia.[4] A high proportion of the analyzed ESBL-EC strains were susceptible to fosfomycin. Interestingly, only 25% of the FR *E. coli* isolates were ESBL-EC suggesting that the *fosA* genes are not spread in our environment. However, this could change in case of dissemination of the *fosA3* genes, which have already been detected in Europe.[10]

We found that older age, dementia and FQ consumption were associated to FR. Nursing home residence has been described as a predictor of FR in ESBL-EC.[6] Further studies are required to fully evaluate the risk factors of FR in *E. coli*.

Our study suggests that FR has not increased over time. Most *E. coli* isolates were FS including ESBL-EC. Risk factors for FR should be considered when prescribing fosfomycin to males with a FUTI.

References

1. Ulleryd P. Febrile urinary tract infection in men. Int J Antimicrob Agents. 2003; Suppl. 2:89–93.
2. Lipsky BA, Byren I, Hoey CT. Treatment of bacterial prostatitis. Clin Infect Dis. 2010;50:1641–52.
3. Smithson A, Ramos J, Bastida MT, Bernal S, Jove N, Niño E, et al. Differential characteristics of healthcare-associated compared to community acquired febrile urinary tract infections in males. Eur J Clin Microbiol Infect Dis. 2015;34:2395–402.
4. Sastry S, Doi Y, Fosfomycin:. Resurgence of an old companion. J Infect Chemother. 2016;22:273–80.
5. Los-Arcos I, Pigrau C, Rodríguez-Pardo D, Fernández-Hidalgo N, Andreu A, Larrosa N, et al. Long-term fosfomycin-tromethamine oral therapy for difficult-to-treat chronic bacterial prostatitis. Antimicrob Agents Chemother. 2015;60:1854–8.
6. Oteo J, Bautista V, Lara N, Cuevas O, Arroyo M, Fernández S, et al. Parallel increase in community use of fosfomycin and resistance to fosfomycin in extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli*. J Antimicrob Chemother. 2010;65:2459–63.
7. Rodríguez-Avial C, Rodríguez-Avial I, Hernández E, Picazo JJ. Increasing prevalence of fosfomycin resistance in extended-spectrum-beta-lactamase-producing *Escherichia coli* urinary isolates (2005–2009–2011). Rev Esp Quimioter. 2013;26:43–6.
8. Pourbaix A, Guerin F, Lastours V, Chau F, Auzou M, Boulley E, et al. Biological cost of fosfomycin resistance in *Escherichia coli* in a murine model of urinary tract infection. Int J Med Microbiol. 2017;307:452–9.
9. Asencio Egea MÁ, Huertas Vaquero M, Carranza González R, Herráez Carrera Ó, Redondo González O, Arias Arias Á. Trend and seasonality of community-acquired *Escherichia coli* antimicrobial resistance and its dynamic relationship with antimicrobial use assessed by ARIMA models. Enferm Infecc Microbiol Clin. 2017, http://dx.doi.org/10.1016/j.eimc.2017.10.013.
10. Benzerara Y, Gallah S, Hommeril B, Genel N, Decré D, Rottman M, et al. Emergence of plasmid-mediated fosfomycin-resistance genes among *Escherichia coli* isolates, France. Emerg Infect Dis. 2017;23:1564–7.

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2529-993X/

Fatal multi-drug-resistant *Acinetobacter baumannii* pneumonia in Maputo, Mozambique: A case report

Neumonía con desenlace fatal por Acinetobacter baumannii *multirresistente en Maputo, Mozambique: reporte de un caso*

Acinetobacter baumannii is one of the six most important multidrug-resistant (MDR) microorganisms isolated in hospitalised patients worldwide, having an extraordinary capacity to spread to different areas.[1] In the last three decades *A. baumannii* has acquired resistance to antibiotics including carbapenems and even polymyxins, representing a challenge for achieving effective antibacterial treatment.[1,2] In the global priority list of antibiotic-resistant bacteria of the World Health Organisation, *A. baumannii* is considered the most critical pathogen.[3] Knowledge of the epidemiology and antibacterial susceptibility profile of *A. baumannii* is still incomplete in many parts of the world including Africa. Here, we report a fatal pulmonary infection by MDR *A. baumannii* in Maputo, Mozambique.

In 2014, a woman in her 20s, with HIV infection on antiretroviral treatment for the preceding 12 months, was admitted to the Maputo Central Hospital with cough, dyspnoea and seizures of acute presentation. Physical examination revealed: a Glasgow score of 15/15, temperature 38.2 °C, blood pressure 180/120 mmHg, heart rate 100 bpm, and respiratory rate 24 rpm. Thick and thin smear tests for malaria were negative. Laboratory analyses during hospitalisation showed anaemia (haematocrit 24.9% and haemoglobin 8.3 g/dL), leukopenia (white blood cell count 2.9×10^9/L), elevated transaminases (AST 157 IU and ALT 726 IU), and kidney failure (maximum creatinine and urea levels were 363 μM/L and 29.4 μM/L respectively); the estimated glomerular filtration (Cockcroft-Gault Equation) was 18.8 mL/min. Chest X-ray was performed and only a cardiomegaly was reported. The nadir CD4 count was 192 cells/mL. Sputum Gram stain and blood culture were not performed. The patient received penicillin, cotrimoxazole, and oxygen but died on day 14 of hospitalisation. Pre-mortem clinical diagnoses were: HIV/AIDS, Kaposi's sarcoma, dilated cardiomyopathy, kidney failure, and pulmonary hypertension. The patient was not intubated or in mechanical ventilation.

The case was included in the CaDMIA project, a validation study of a minimally invasive autopsy (MIA) protocol against the complete diagnostic autopsy (CDA).[4,5] A universal screening for

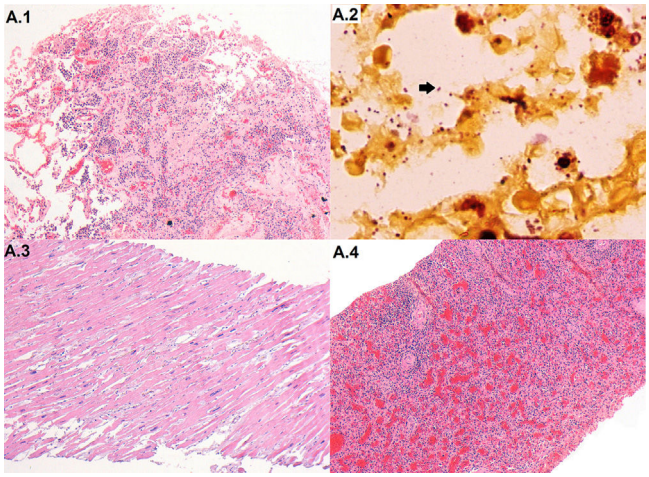

Fig. 1. Fatal MDR *A. baumannii* infection: microbiological and pathological results of post-mortem samples.
Histological images of relevant findings. (A.1) Lung with pyogenic pneumonia (haematoxylin and eosin, 100×); (A.2) Gram negative bacteria (*A. baumannii*) pneumonia (arrow) infecting the lung (gram stain, 1000×); (A.3) heart with hypertrophy (haematoxylin and eosin, 100×); (A.4) spleen with lymphocytic depletion and congestion (haematoxylin and eosin, 100×).

several key pathogens was conducted, and microbiological analysis were performed according to the histopathological findings.[4,5] The autopsy revealed a severe pyogenic pneumonia (Fig. 1). Serum samples tested positive for antibodies against HIV with a viral load of 182 copies/mL. Lung samples resulted negative for tuberculosis, *Cryptococcus*, *Toxoplasma gondii*, *Pneumocystis jirovecii* and respiratory viruses by PCR testing. *A. baumannii* was isolated from brain, lung and liver samples. Gram negative bacilli were visible in the Gram stain of histological lung samples (Fig. 1), brain, and liver. *A. baumannii* was also identified by 16S rRNA PCR in plasma, brain, lung, liver and cerebrospinal fluid samples. The cause of death was assigned to fatal pneumonia caused by a MDR *A. baumannii* infection, following a previously described algorithm.[6] Clinical diagnosis of Kaposi's sarcoma and dilated cardiomyopathy were not confirmed at autopsy.

Antibiotic susceptibility tests were performed and interpreted according to the EUCAST guidelines (version 7.0,2017; http://www.eucast.org) which consider *A. baumannii* intrinsically resistant to penicillins and cephalosporins. In addition, the strain was resistant to the following antibiotics: ciprofloxacin, levofloxacin, trimethoprim-sulphamethoxazole, and gentamicin; showing intermediate resistance to meropenem (4 μg/mL) and susceptibility to amikacin, tobramycin, imipenem and colistin. The MIC of tigecycline was 1 μg/mL. Multi-Locus Sequence Typing following the Pasteur scheme (https://pubmlst.org/abaumannii/) identified all the *A. baumannii* isolates as belonging to international clone II and sequence type 2(ST2).

Few data are available in the literature regarding *A. baumannii* in Africa. A recent report analysed 65 strains from 5 different countries and found a high prevalence of MDR strains.[7] International clone II/ST2 isolates belong to one of the major clonal lineages associated with the spread of MDR *A. baumannii* worldwide, but in Africa they have only been reported in Algeria and Kenya.[8,9] Two recent studies[10,11] (one of them conducted at the Maputo Central Hospital) reported non-MDR *A. baumannii* in Mozambique, whereas, to our knowledge, this is the first report of a MDR *A. baumannii* strain in this country. The patient had several known risk factors for acquiring *A. baumannii* infection such as severe immunosuppression and having been hospitalised for two weeks. However, the final cause of death was only identified after a complete diagnostic autopsy and in depth microbiological studies were carried out. Diagnostic autopsies are rarely performed in sub-Saharan Africa due to, among others, the lack of resources and trained pathologists. We show that a standardised minimally invasive sampling procedure can provide accurate identification of a pathogen causing death. This method may improve the capacity of the current surveillance methods to detect bacterial infections and associated antimicrobial resistance. Our report highlights the utility of post-mortem investigations for accurate determination of cause of death and the need for microbiological surveillance to tackle the growing problem of nosocomial MDR infections in low-income countries.

Availability of data and material

All relevant data are within the paper. Any additional data use and transfer is monitored by ISGlobal Data Management and Biostatistics Unit (contact e-mail: ubioesdm@isglobal.org).

Ethics approval and consent to participate

The study protocol received approval from the National Mozambican Ethics Committee (ref.342/CNBS/13) and the Ethics Committee of the Hospital Clinic of Barcelona (Spain; approved, File 2013/8677). The MIA and CDA procedures were only conducted after verbal informed consent was provided by the relatives.

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Appendix A.

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References

1. Roca I, Espinal P, Vila-Farres X, Vila J. The *Acinetobacter baumannii* Oxymoron: commensal hospital dweller turned pan-drug-resistant menace. Front Microbiol. 2012;3:148, http://dx.doi.org/10.3389/fmicb.2012.00148.
2. Karah N, Sundsfjord A, Towner K, Samuelsen Ø. Insights into the global molecular epidemiology of carbapenem non-susceptible clones of *Acinetobacter baumannii*. Drug Resist Updates. 2012;15:237–47, http://dx.doi.org/10.1016/j.drup.2012.06.001.
3. World Health Organization. Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. Available at: http://www.who.int/medicines/publications/global-priority-list-antibiotic-resistant-bacteria/en/ [accessed 16.03.17].
4. Castillo P, Ussene E, Ismail MR, Jordao D, Lovane L, Carrilho C, et al. Pathological methods applied to the investigation of causes of death in developing countries: minimally invasive autopsy approach. PLOS ONE. 2015;10:e0132057, http://dx.doi.org/10.1371/journal.pone.0132057.

5. Martínez MJ, Massora S, Mandomando I, Ussene E, Jordao D, Lovane L, et al. Infectious cause of death determination using minimally invasive autopsies in developing countries. Diagn Microbiol Infect Dis. 2016;84:80–6, http://dx.doi.org/10.1016/j.diagmicrobio.2015.10.002.
6. Castillo P, Martínez MJ, Ussene EA, Jordao D, Lovane L, Ismail MR, et al. Validity of a minimally invasive autopsy for cause of death determination in adults in Mozambique: an observational study. PLoS Med. 2016;13:e1002171, http://dx.doi.org/10.1371/journal.pmed.1002171.
7. Lob SH, Hoban DJ, Sahm DF, Badal RE. Regional differences and trends in antimicrobial susceptibility of *Acinetobacter baumannii*. Int J Antimicrob Agents. 2016;47:317–23, http://dx.doi.org/10.1016/j.ijantimicag.2016.01.015.
8. Bakour S, Touati A, Bachiri T, Salhi F, Touit D, Naim M. First report of 16S rRNA methylaseArmA-producing *Acinetobacter baumannii* and rapid spread of metallo-beta-lactamase NDM-1 in Algerian hospitals. J Infect Chemother. 2014;20:696–701, http://dx.doi.org/10.1016/j.jiac.2014.07.010.
9. Revathi G, Siu LK, Lu PL, Huang LY. First report of NDM-1-producing *Acinetobacter baumannii* in East Africa. Int J Infect Dis. 2013;17:e1255–8, http://dx.doi.org/10.1016/j.ijid.2013.07.016.
10. Le Doare K, Bielicki J, Heath PT, Sharland M. Systematic review of antibiotic resistance rates among Gram-negative bacteria in children with sepsis in resource-limited countries. J Pediatr Infect Dis Soc. 2015;4:11–20, http://dx.doi.org/10.1093/jpids/piu014.
11. Preziosi M, Zimba TF, Lee K, Tomas M, Kinlin S, Nhatave-Paiva C. A prospective observational study of bacteraemia in adults admitted to an urban Mozambican hospital. S Afr Med J. 2015;105:370–4, http://dx.doi.org/10.7196/samj.8780.

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2529-993X/

Epidemiological analysis of acute respiratory infections caused by enterovirus D68 clade A, subclade A1 in the adult population☆

Análisis epidemiológico de las infecciones respiratorias agudas causadas por el enterovirus D68 clado A, subclado A1 en la población adulta

Enterovirus D68 (EV-D68) is a virus belonging to species D of the genus *Enterovirus* within the *Picornaviridae* family. It was first described in 1962 in California as rhinovirus 87 and cause of paediatric respiratory infections.[1] In 2014, a significant epidemic of respiratory infections caused by EV-D68 was reported in the United States, affecting more than 1100 patients, in some cases associated with neurological complications.[2] As a result of this situation, a number of different countries, including France, Italy, the Netherlands, Germany and other European countries, began to look for this virus in both paediatric and adult respiratory infections.[3,4]

In Spain, some isolated cases of community-acquired and hospital-acquired acute respiratory infection associated with EV-D68 have been reported in the adult population and in children.[5,6] Because of the distinct lack of information regarding this disease in adults, we decided to analyse the epidemiological characteristics of the 12 cases of acute respiratory infection associated with EV-D68 recently detected.

In December 2017 and January 2018, 1050 respiratory samples from adult patients were processed. Each of them was subjected to real-time commercial PCR (RT-PCR) (Allplex Respiratory Full Panel Assay, Seegene, South Korea) for the detection of respiratory viruses.

During this time, 651 positive samples were detected (62%). These comprised 37 enteroviruses (5.6%), 12 (32.4%) of which were identified as EV-D68 clade A, subclade A1 at the *Centro Nacional de Enterovirus* [Spanish Enterovirus Centre] in Madrid through RT-nested PCR and sequencing of the 3-VP1 region of the virus.[6] These 12 enteroviruses represented 1.8% of the positive samples and 1% of the total analysed.

The main clinical and epidemiological characteristics of these patients are shown in Table 1. Most of the respiratory infections were mild or moderate or flu-like; only two patients (16.6%) required admission to the ICU, one as a result of a severe asthma attack and the other a flu-like episode with respiratory distress. The mean age of our patients (52.8 years) was older than that reported in another study (36.7 years).[7] In the Meijer et al. study,[8] 28% of the adult cases were in the 40–59 age group. None of the patients died and all were discharged from hospital without any sequelae of note.

We compared our incidence data with those reported by other authors and found that the 21 cases of EV-D68 in adults in the Schuffenecker et al. study[4] in France in 2014 only represented 10.6% of all isolates and their clinical characteristics were similar to those in our study. Three of their patients were admitted to the ICU (14.2%) and four (19%) had pneumonia (8.3% in our study). In Germany, in 2013–2014 Böttcher et al.[3] found that EV-D68 represented 0.3% of all respiratory samples, but they do not specify to which age groups they belonged. Other studies hardly report any cases in adults: Lu et al.[9] detected two cases (22%) of EV-D68 in adults with

Table 1
Main characteristics of the 12 adult patients with EV-D68 detected in the respiratory tract.

Male, n (%)	6 (50)
Female, n (%)	6 (50)
Mean age, years (range)	52.8 (16–75)
Hospital admission, n (%)	6 (50)
Transfer ICU, n (%)	2 (16.6)
Antibiotic therapy, n (%)	8 (66.6)
Symptoms, n (%)	
Pyrexia	11 (91.6)
Cough	10 (83.3)
General malaise	6 (50)
Myalgia	5 (41.6)
Pharyngitis	5 (41.6)
Headache	3 (25)
Dyspnoea	2 (16.6)
Clinical diagnosis, n (%)	
Influenza	4 (33.3)
Acute respiratory infection	3 (25)
Asthma	2 (16.6)
Pneumonia	1 (8.3)
Bronchitis	1 (8.3)
COPD	1 (8.3)

COPD: chronic obstructive pulmonary disease; ICU: intensive care unit.

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