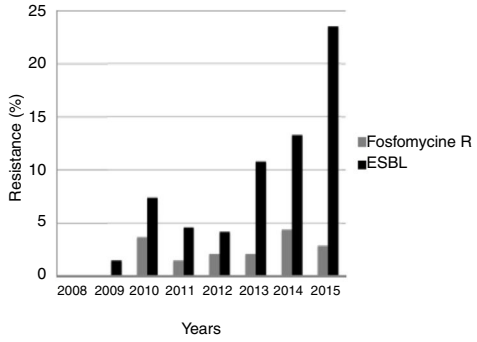

Fig. 1. Trends in fosfomycin resistance and ESBL production in *E. coli* isolated from males with febrile urinary tract infection over the study period.
Abbreviations: R: resistant; ESBL: extended-spectrum beta-lactamase.

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.

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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 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,

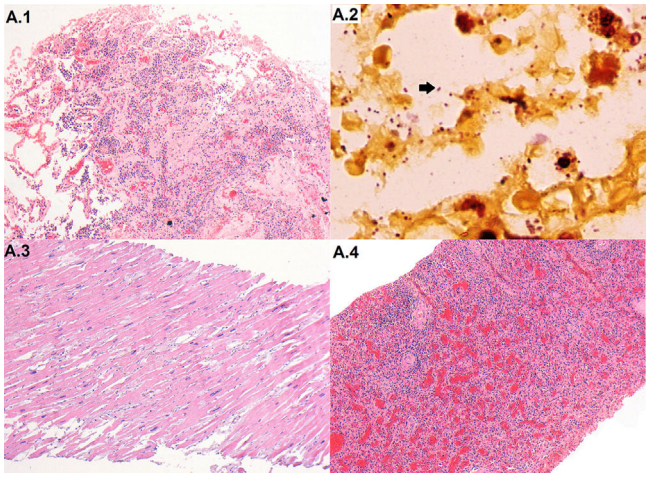

Fig. 1. Fatal MDR *A. baumannii* infection: microbiological and pathological results of post-mortem samples.
Histological images of relevant findings. (A.1) Lung with pyogenic pneumonia (haematoxylin and eosin, 100×); (A.2) Gram negative bacteria (*A. baumannii*) pneumonia (arrow) infecting the lung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

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

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

El enterovirus D68 (EV-D68) es un virus que pertenece a la especie D del género *Enterovirus* dentro de la familia *Picornaviridae*. Fue descrito por primera vez en 1962 en California como rinovirus 87 y causante de infecciones respiratorias pediátricas[1]. En 2014 se comunicó en Estados Unidos una importante epidemia de infecciones respiratorias causadas por el EV-D68 afectando a más de 1.100 pacientes, en ocasiones asociadas a complicaciones neurológicas[2]. A raíz de esta situación diferentes países iniciaron la búsqueda de este virus en las infecciones respiratorias, tanto pediátricas como de adultos, habiéndose descrito en Francia, Italia, Holanda y Alemania, entre otros países europeos[3,4].

En nuestro país se han comunicado algunos casos aislados de infección respiratoria aguda asociados al EV-D68 tanto en población adulta como en niños comunitarios y hospitalizados[5,6]. La escasa información referente a esta patología en adultos nos ha llevado a analizar las características epidemiológicas de los 12 casos de infección respiratoria aguda asociados al EV-D68 detectados recientemente.

Durante los meses de diciembre de 2017 y enero de 2018 se procesaron 1.050 muestras respiratorias de pacientes adultos. A cada uno de ellos se les realizó la detección de virus respiratorios mediante una RT-PCR comercial en tiempo real (Allplex Respiratory Full Panel Assay; Seegen, Corea del Sur).

En este período se detectaron 651 muestras positivas (62%) y en ellas 37 enterovirus (5,6%) de los cuales 12 (32,4%) fueron identificados como EV-D68 clado A, subclado A1 en el Centro Nacional de Enterovirus (Madrid) mediante una RT-nested para la región 3ᶜVP1 del virus y posterior secuenciación del mismo[6]. Estos 12 enterovirus representaron el 1,8% de las muestras positivas y el 1% del total de las analizadas.

Las principales características clínicas y epidemiológicas de estos pacientes se presentan en la tabla 1. La mayoría de las infecciones respiratorias fueron leves o moderadas o cuadros gripales; solo dos pacientes (16,6%) requirieron del ingreso en la UCI como consecuencia de una crisis asmática intensa y un cuadro gripal con distrés respiratorio. La edad media de nuestros pacientes (52,8 años) fue superior a la comunicada en otro estudio (36,7 años)[7]. En el estudio de Meijer et al.[8] el 28% de los casos en adultos tenían una edad situada entre los 40-59 años. Ningún paciente falleció y todos fueron dados de alta sin secuelas valorables.

Cuando se comparan nuestros datos de incidencia con los comunicados en otros estudios se observa que en Francia en 2014 Schuffenecker et al.[4] detectan que los 21 EV-D68 en adultos solo representan el 10,6% de todos los aislados y que sus características clínicas son semejantes a las observadas en nuestro estudio. Así 3 pacientes ingresaron en la UCI (14,2%) y 4 (19%) presentaron neumonía (8,3% en nuestro estudio). En Alemania Böttcher et al.[3] han observado entre los años 2013-2014 que el EV-D68 representa el 0,3% de todas las muestras respiratorias aunque no se especifica a qué grupos de edad corresponden. En otros estudios apenas se comunican casos en adultos, así Lu et al.[9] detectan 2 (22%) en el período 2009 y 2012 casos de EV-D68 en adultos con patología respiratoria leve; mientras que Zhang et al.[10] entre 2011 y 2015 solo detectan un caso, representando el 18% de todos los aislados. En el estudio comparativo entre la circulación del EV-D68 entre Europa y Estados Unidos realizado por Poelman et al.[11] en 2015 se confirma la baja prevalencia de este virus en Europa y su menor morbilidad durante el brote norteamericano. En España en 2014 Gimferrer et al.[5] fueron los primeros en comunicar 2 (40%) casos en adultos, en un grupo de 5 pacientes ingresados, sin necesidad de ingreso en la UCI.

En ninguno de estos estudios se han podido detectar en los adultos afectaciones neurológicas graves o parálisis flácidas como se ha

Tabla 1
Principales características de los 12 pacientes adultos con detección de EV-D68 en el tracto respiratorio

Hombre, n (%)	6 (50)
Mujer, n (%)	6 (50)
Edad media, años (rango)	52,8 (16-75)
Ingreso hospital, n (%)	6 (50)
Ingreso UCI, n (%)	2 (16,6)
Tratamiento antibiótico, n (%)	8 (66,6)
Síntomas, n (%)	
Fiebre	11 (91,6)
Tos	10 (83,3)
Malestar general	6 (50)
Mialgias	5 (41,6)
Faringitis	5 (41,6)
Cefalea	3 (25)
Disnea	2 (16,6)
Diagnóstico clínico, n (%)	
Gripe	4 (33.3)
Infección respiratoria aguda	3 (25)
Asma	2 (16.6)
Neumonía	1 (8.3)
Bronquitis	1 (8.3)
EPOC	1 (8.3)

EPOC: enfermedad pulmonar obstructiva crónica; UCI: unidad de cuidados intensivos.