Journal of Global Antimicrobial Resistance 22 (2020) xxx–xxx

Contents lists available at ScienceDirect

Journal of Global Antimicrobial Resistance

journal homepage: www.elsevier.com/locate/jgar

A five-year retrospective study shows increasing rates of antimicrobial drug resistance in Cabo Verde for both *Staphylococcus aureus* and *Escherichia coli*

Tamar Monteiro[a,&], Magdalena Wysocka[b,c,&], Elena Tellez[d], Ofelia Monteiro[d], Luzia Spencer[d], Elisa Veiga[d], Sandra Monteiro[e], Carine de Pina[a], Deisy Gonçalves[a], Sandrine de Pina[a], Antonio Ludgero-Correia[a], Joao Moreno[a], Teresa Conceição[f], Marta Aires De Sousa[f], Herminia de Lencastre[f,g], Laura J Gray[h], Manish Pareek[i], David R. Jenkins[j], Sandra Beleza[b], Marco R. Oggioni[b,*], Isabel Inês Araujo[a], on behalf of the ANCoVer project[1]

[a] *Faculdade de Ciências e Tecnologia, Universidade de Cabo Verde, Praia, Santiago, Cabo Verde*
[b] *Department of Genetics and Genome Biology, University of Leicester, Leicester, UK*
[c] *Department of Molecular Biotechnology and Microbiology, Gdansk University of Technology, Gdansk, Poland*
[d] *Hospital Agostinho Neto, Ministério da Saúde e Segurança Social, Praia, Santiago, Cabo Verde*
[e] *Hospital Baptista de Sousa, Ministério da Saúde e Segurança Social, Mindelo, São Vicente, Cabo Verde*
[f] *Laboratory of Molecular Genetics, Instituto de Tecnologia Química e Biológica António Xavier (ITQB-NOVA), Universidade Nova de Lisboa, Oeiras, Portugal*
[g] *Laboratory of Microbiology & Infectious Diseases, The Rockefeller University, New York, USA*
[h] *Department of Health Sciences, University of Leicester, Leicester, UK*
[i] *Department of Respiratory Sciences, University of Leicester, Leicester, UK*
[j] *Department of Clinical Microbiology, University Hospitals of Leicester, NHS Trust, Leicester, UK*

ARTICLE INFO

Article history:
Received 18 December 2019
Received in revised form 31 March 2020
Accepted 3 April 2020
Available online 27 April 2020

ABSTRACT

Objectives: Data on baseline drug resistance important in informing future antimicrobial stewardship programs. So far, no data on the antimicrobial drug resistance of clinical isolates available for the African archipelago of Cabo Verde.

Methods: We performed a retrospective analysis over years (2013-17) of the drug susceptibility profiles of clinical isolates in the two main hospitals of Cabo Verde. For *Escherichia coli* and *Staphylococcus aureus*, representing 47% and 26% of all clinical isolates, the antimicrobial drug resistance profile was reported for six representative drugs.

Results: For *E. coli* we detected an increase in resistance to ampicillin, amoxicillin/clavulanic acid, ceftriaxone, ciprofloxacin and trimethoprim-and for *S. aureus* to methicillin, erythromycin and trimethoprim-sulfamethoxazole. This increase in both the most commonly isolated bacterial pathogens is alarm as it might compromise empirical treatment in a setting with limited access to laboratory testing.

Conclusions: When compared to the published low resistance rates in carriage isolates, the more alarming situation in clinical isolates for *S. aureus* might encourage antimicrobial stewardship programs to reduce in hospital settings, possibly as part of the Cabo Verdean national plan against antimicrobial drug resistance.

1. Introduction

The global burden of antimicrobial-resistant infections is growing at an alarming rate, being responsible for more than half a million deaths worldwide each year [1,2,3]. In the absence of effective control interventions, annual number of deaths related to resistance may rise to 10 million per year by 2050, according to a UK government commissioned review [3], although others have

* Corresponding author.
E-mail address: mro5@leicester.ac.uk (M.R. Oggioni).
[&] authors contributed equally to work
[1] The ANCoVer project includes Antonieta Martins, Deisa Semedo, Eliane Swely Sanches, Mayra Monteiro, Maria da Luz Lima,Miriam Pereira, Natalina Spencer, Tatiana Cardoso, Caroline Kristunas and Mark Goodwin

http://dx.doi.org/10.1016/j.jgar.2020.04.002

forecast lower numbers, particularly in parts of the world where non-antimicrobial measures can be implemented to prevent infectious disease mortality [4]. These projections both the international burden and local variation in resistance rates. Several reviews have highlighted the impact of international travel, including immigration, on the worldwide spread of resistant bacteria, to countries that are effectively controlling their antibiotic use [3,5,6].

The resistance crisis has prompted a rise in antimicrobial stewardship (AMS) programs which aim to reduce inappropriate antibiotic use. Although AMS focuses on antibiotic prescribing practice, it is underpinned by an understanding of local antibiotic susceptibility patterns, which in turn depends on the availability of a reliable medical microbiology laboratory resource. In light of the crisis of antimicrobial drug resistance (AMR), the implementation of clinical bacteriology laboratories in low-resource settings improves patient management, delivering both guidance for individual patient infection management and surveillance for support of antibiotic treatment guideline and policies [6,7].

Cabo Verde (CV) is a sovereign nation composed of 10 islands located in the Atlantic Ocean west of Senegal, with a population in 2016 of 539,560 [8]. In 2017, infectious diseases were the second highest cause of death, reflecting economic development [9]. Human antibiotic use is based largely on empirical prescribing and is generally restricted to a small number of relatively narrow spectrum antibiotics [9]. International travel to and from the islands is relatively high; large numbers of the Cabo Verdean population have emigrated, predominantly to Europe (majority in Portugal, France and Netherlands) and the and they pay return visits to their homeland immigrants from mainland Africa, especially other lusophone countries make up 2.9% of the population in 2010 and there are increasing numbers of tourists, including from countries with high rates of antibiotic resistance [10]. Additionally, Cabo Verdean patients may have to travel to Europe for tertiary care, potentially to hospitals with endemic multidrug resistance problems. Consequently, despite modest antibiotic use in CV, concern about resistance has prompted the implementation of infection control measures [11] and, in 2018, the CV government launched a national plan against [9].

Although data on carriage isolates of *S aureus* in CV were reported to show very low levels of methicillin resistance [12], the overall level of AMR in clinical isolates has not been previously investigated. The aim of the present study was to characterise the antimicrobial drug susceptibility of the most frequently isolated clinical pathogens in the two hospitals in CV, with the more general goal to inform public health planning and programs.

2. Methods

2.1. Hospitals

Hospital Agostinho Neto (HAN) and Hospital Baptista de Sousa (HBS), the two main public hospitals in Cabo Verde, participated in the retrospective study (see Table S1). HAN is a 400-bed hospital located in the city of Praia, the capital of Cabo Verde, on the island of Santiago. The hospital has a bed occupancy rate of around 80% and receives patients from Santiago and other islands (often from Fogo, Brava, Maio, Sal and Boavista, as well as a few cases from São Vicente, São Nicolau and Santo Antão). HBS is a 220-bed hospital located in the city of Mindelo on the island of São Vicente, and receives patients mainly from Santo Antão and São Nicolau. The clinical laboratories at the two hospitals receive human samples for diagnosis from internal and external patients, living in the islands and from all other islands.

2.2. Data collection

Retrospective microbiology laboratory antimicrobial drug susceptibility data for the time period January 2013 to December 2017 were collected in summer 2018. A total of 5669 positive samples from both hospitals were processed (see Table S1). Of the 3577 positive samples processed at HAN, there were 1818 urine samples, 603 pus samples, 154 blood cultures and 1002 other samples. Of the 2092 positive samples processed at HBS there were 1716 urine samples, 88 pus samples, 64 blood cultures and 224 other samples. From these specimens, 1252 *S. aureus* isolates were cultured at HAN and 204 at HBS. The corresponding numbers of *E coli* isolates were 1753 from HAN and 882 from HBS from all samples and 1539 and 868 from urine respectively (Table S1).

2.3. Phenotypic

At both HAN and HBS *S. aureus* was isolated on mannitol salt agar plates (Oxoid) and identified using Pastorex Staph-Plus (Bio-Rad) while *E. coli* was isolated on Eosin Methylene Blue (EMB) agar plates (Oxoid) and in selected cases identity was confirmed using API 20E (Biomerieux). Antimicrobial susceptibility testing discs were from Oxoid and inhibition zones were interpreted using breakpoints [13].

2.4. Statistical analysis

Categorical variables were using the frequency and percentage. The chi-square test was used to identify differences between susceptibility proportions among islands and regions. The chi-square test for trend in proportions was used to evaluate trends in the *S. aureus* and *E. coli* resistance rates per year. In all cases, values of $\leq$0.05 were considered statistically significant and analysis was conducted using R software version 3.5.1.

3. Results

In the 5-year period 2013-17, the microbiology laboratories of the two hospitals HAN and HBS in reported 5669 positive samples, of which 1456 were positive for *S. aureus* (25.7%), 1252 for HAN and 204 for HBS. The distribution of isolated strains according to the type of sample is given in Table S1. Susceptibility testing of *S. aureus* for all type of samples from HAN showed resistance to penicillin for 95.1% of isolates, to methicillin (oxacillin) 15.8%, erythromycin 18.9%, chloramphenicol 4.6%, ciprofloxacin 10.2%, trimethoprim-17.4% and tetracycline 9.7% (Fig. 1aa). Among *S. aureus* all type of samples from HBS, we noticed resistance to penicillin (87.3%), methicillin (55.1%), erythromycin (48.4%), chloramphenicol (22.4%), ciprofloxacin (27.4%), trimethoprim-(35.7%) and tetracycline (35.1%) (Fig. 1a).

The proportions of resistant bacteria were broken down for the study period (2013-2017). A statistically significant trend was found in *S. aureus* isolates in Santiago between 2013 and 2017 for methicillin (oxacillin; <0.0001), penicillin (0.032) and erythromycin (0.022). For the other antibiotics, there was no increase in drug resistance over time (>0.05) (Fig. 1b). A statistically significant trend was found in *S. aureus* isolates in São Vicente between 2013 and 2017 for four antibiotics: penicillin resistance rate decreased (0.0062), chloramphenicol resistance rate decreased (0.0031), trimethoprim-resistance rate increased (0.018) and methicillin resistance rate increased (0.0007). The ciprofloxacin and erythromycin resistance rate decreased 2013-16 to increase in 2017 (>0.05) (Fig. 1c). It should be noted that the sample size is low for some antibiotics in certain years due to issues linked to the supply of susceptibility testing discs (Fig. S1, Table S2S3).

We found significant differences between islands (Fig. 1a): in Santiago we observed higher resistance to penicillin (95.1% vs 87.3%, 0.005); in São Vicente we observed higher resistance to

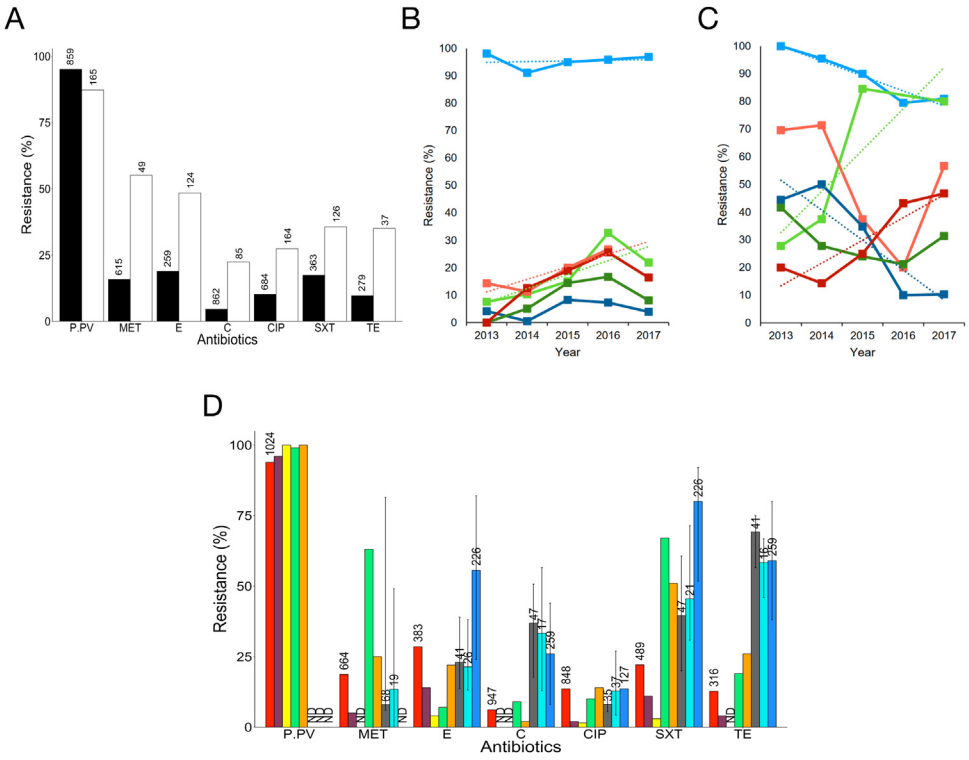

Fig. 1. Antimicrobial resistance among *S aureus* isolates (A) in all type of samples between Santiago (HAN) (black) and São Vicente (HBS) (white). Bars represent percentages of resistancethe bars the number of tested strains in all type of samples for each island. (B) Trends in the proportions of antibiotic resistance from 2013 to 2017 in Santiago (HAN) (B) and 2014 to 2017 in São Vicente (HBS) (C). The chi-square analysis was applied to test the trends. For details of data see Fig. 1 and Table S2S3. Observed proportions are presented as solid lines for penicillin (blue), methicillin (light green), erythromycin (orange), chloramphenicol (deep blue), ciprofloxacin (deep green), trimethoprim-(red) and the statistically significant trends are shown as a dotted line (a0.05). (D) AMR among S. *aureus* for different specimens and region of Africa: Cabo Verde (pink[14], yellow[15]), Angola[14] green), São Tomé and Príncipe[14] orange), Eastern Africa[16] grey), Western Africa[16] cyan) and Central/Southern Africa[16] blue). Antibiotics are penicillin, methicillin, erythromycin, chloramphenicol, ciprofloxacin, trimethoprim-and tetracycline. For three of the studies in D the median prevalence of resistance against relevant antimicrobial drugs with interquartile range is given.

methicillin (55.1% vs 15.8%, <0.0001), erythromycin (48.4% vs 18.9%, <0.0001), chloramphenicol (22.4% vs 4.6%, <0.0001), ciprofloxacin (27.4% vs 10.2%, <0.0001), trimethoprim-(35.7% vs 17.4%, 0.001) and tetracycline (35.1% vs 9.7%, 0.001) (Table S4).

To place the data of in clinical samples from CV into an international context, we compared our data to data from two carriage studies from the same two hospitals in CV [14,15] and global resistance surveys in Africa [16,17]. Compared to other countries, we found in Angola higher resistance to trimethoprim-(66.5%) and methicillin (63.0%); in São Tomé and Príncipe higher resistance to trimethoprim-(51.0%) and tetracycline (26.0%).

We used median prevalence of resistance with Interquartile range (IQR) from a systematic review to compare our results to the regions of Africa and we noticed the following (Fig. 1d): in Western Africa for *S. aureus* isolated from patients with a febrile illness, the median prevalence of resistance to tetracycline (58.3%; between 46.0% and 66.7%) and notable resistance to trimethoprim-(45.5%; between 30.8% and 71.4%) chloramphenicol (33.3%; between 12.9% and 56.5%); in Eastern sub-Sahara Africa, the high median prevalence of resistance to tetracycline in *S. aureus* isolated from patients with a febrile illness (69.2%; between 56.5% and 74.9%) as well as to trimethoprim-(39.6%; between 20.0% and 60.6%) and chloramphenicol (36.9%; between 17.7% and 50.7%); in Central/Southern Africa, high median prevalence of resistance to trimethoprim-(80.0%; between 51.8% and 92.0%) in *S. aureus* isolated from patients with a febrile illness, but to tetracycline (59.0%; between 38.0% and 80.0%) chloramphenicol (26.0%; between 8.0% and 44.0%) and erythromycin (55.6%; between 24.0% and 82.0%). We noticed the absence of data on resistance to penicillin from around the African region [16].

E. coli was the most frequent bacterium isolated in both hospitals (2635, 46.5%) 1753 for HAN and 882 for HBS. The most common type of samples for *E. coli* were urine (2407, 91.4%) for both hospitals (Table S1). Among the 1539 *E. coli* urine samples from HAN, we documented resistance to ampicillin (78.9%), amoxicillin/clavulanic acid (20.1%), ceftriaxone (28.2%), ciprofloxacin (30.3%), trimethoprim-sulfamethoxazole (60.5%) and gentamicin (21.6%) (Fig. 2aa). Among the 868 *E. coli* urine samples from HBS, we found resistance to ampicillin (73.3%), amoxicillin/clavulanic acid (48.6%), ceftriaxone (15.6%), ciprofloxacin (18.7%), trimethoprim-(44.0%) and gentamicin (21.2%) (Fig. 2a).

We found statistically significant increases in resistance in `*E. coli* isolates HAN between 2013 and 2017 for ampicillin (0.005), amoxicillin/clavulanic acid (0.016), ceftriaxone (<0.0001), nalidixic acid (<0.0001), ciprofloxacin (0.004) and trimethoprim-(0.011) (Fig. 2) (Fig. S1, Table S5). For HBS between 2013 and 2017, we found decreased resistance for ampicillin (<0.0001) and increased resistance for ciprofloxacin (0.029) and ceftriaxone (0.008) (Fig. 2b) (Fig. S1, Table S6). At HAN also cefuroxime susceptibility decreased in the same measure as ceftriaxone (data not shown), with both data being compatible with an increase extended spectrum beta-lactamase (ESBL) positive *E. coli* in Cabo Verde.

We found significant differences between islands (Fig. 2a): in São Vicente we observed high levels of resistance to amoxicillin/clavulanic acid relative to Santiago (48.6% vs 20.1%, <0.0001); in Santiago we noticed statistically significant higher levels of resistance relative to São Vicente for ceftriaxone (28.2% vs 15.6%, <0.0001), ciprofloxacin (30.3% vs 18.7%, <0.0001) trimethoprim-(60.5% vs 44.0%, <0.0001). There was no significant difference

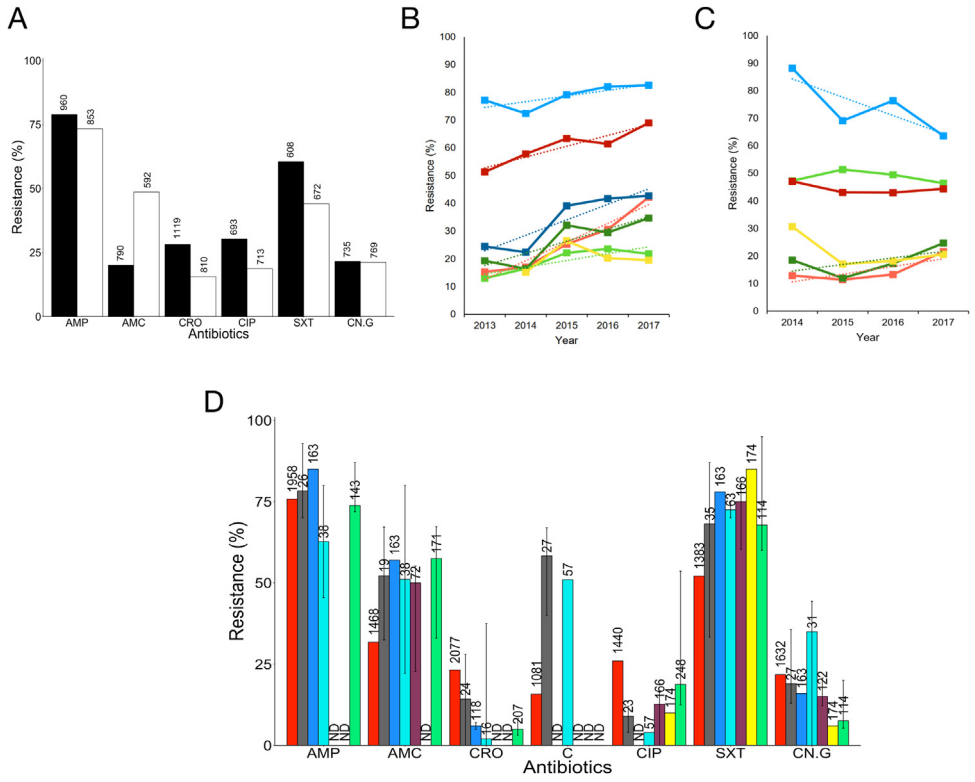

Fig. 2. Antimicrobial resistance among *E coli* isolates. (A) in urine samples between Santiago (HAN) (black) and São Vicente (HBS) (white). Bars represent percentages of resistance the bars the number of tested strains in urine samples for each island. Antibiotics: ampicillin, amoxicillin/clavulanic acid, ceftriaxone, nalidixic acid, ciprofloxacin, trimethoprim-and gentamicin. (B) Trends in the proportions of antibiotic resistances from 2013 to 2017 in Santiago (HAN) (B) and 2014 to 2017 in São Vicente (HBS) (C). The chi-square analysis was applied to test the trends. For details of data see Fig. 1 and Table S5S6. Observed proportions are presented as a solid lines for ampicillin (blue), amoxicillin/clavulanic acid (light green), ceftriaxone (orange), nalidixic acid (deep blue), ciprofloxacin (deep green), trimethoprim-(red), gentamicin (yellow) and the statistically significant trends are shown as a dotted line ($\leq$0.05). (D) AMR among *E. coli* for different specimens and region of Africa: Cabo Verde (red), Western Africa[16] (fever cyan urinary tract infectiongreen), Eastern Africa[16] (grey pink) and Central/Southern Africa[16] (blue yellow). Antibiotics are ampicillin, amoxicillin/clavulanic acid, ceftriaxone, chloramphenicol, ciprofloxacin, trimethoprim-and gentamicin. For three of the studies in D the median prevalence of resistance against relevant antimicrobial drugs with interquartile range is given.

between islands for ampicillin and gentamicin (Table S7). Carbapenem susceptibility was not tested.

To compare our results with other regions, we used median prevalence of resistance with IQR against relevant antimicrobial drugs reported for *E. coli* isolated from patients with a community-acquired febrile illness or urinary tract infection in Western, Central/Southern and Eastern sub-Africa [16]. We noticed the following (Fig. 2d): higher median prevalence of resistance to amoxicillin/clavulanic acid, chloramphenicol and trimethoprim-in all noticed regions of Africa; lower median prevalence of resistance to ceftriaxone ciprofloxacin in all noticed regions of Africa; lower median prevalence of resistance to gentamicin in all regions, besides *E. coli* isolated from patients with a community-acquired febrile illness in Western Africa or ampicillin resistance, lower median prevalence of resistance in Western Africa and higher in Central/Southern and Eastern sub-Africa [16].

4. Discussion

This report shows an alarming and recent increase in methicillin-resistant *S. aureus* (MRSA) and ESBL positive *E. coli* infections in by retrospectively analysing the laboratory results of the two main public hospitals of CV located in the capital Praia on the island of Santiago (HAN) and in Mindelo on the island of São Vicente (HBS) for the years 2013-2017. This is the first study on the susceptibility profiles of clinical isolates in CV and focuses on the two most common bacterial pathogens isolated in a hospital setting.

Over the 5-year period of review, the most frequent laboratory isolate from clinical samples, *E. coli*, showed for one of the two hospitals (HAN) an increase in resistance to almost all antimicrobial drugs monitored. This is most likely due to the diffusion of clones carrying ESBL. This trend was not shared by the second hospital (HBS). Still, the cumulative data show an increase in resistance to ampicillin, amoxicillin/clavulanic acid, ceftriaxone, cefuroxime (data not shown), nalidixic acid, ciprofloxacin, norfloxacin (data not shown) and trimethoprim-. This is a worrying trend that requires an urgent local response. Except for a somewhat higher prevalence of ceftriaxone resistance, indicative of gene circulation, the overall situation is comparable to that of other African studies on [16,17].

Analyzing susceptibility profiles of the hospital isolates of *S. aureus* over these years we noted an increase in methicillin (oxacillin) resistance in both hospitals. At HAN, methicillin resistance increased in parallel to an increase in erythromycin and trimethoprim-resistance, while only increase in resistance to trimethoprim-was detected at HBS. In the latter case, this may be due to the low number of samples tested for oxacillin susceptibility at HBS. The concomitant increase in resistance to other drugs in methicillin resistant isolates is in line with the multidrug resistance pattern of some MRSA [18]. When compared to other studies in Africa, the CV data are in line with other reports [12,14,15,16,17]. For *S. aureus,* two studies reported the susceptibility profiles of nasal carriage isolates collected from patients and hospital staff at the two hospitals HAN and HBS in in the years 1997 [12,15] and 2013-14 [14]. For all drugs tested, the clinical isolates showed higher prevalence of resistance

than carriage isolates collected in the same locations and in part during the same period. A lower prevalence of MRSA carriage relative to high MRSA prevalence in clinical isolates is well known [18,19,20], but in this case, the carriage study was performed on nasal isolates of staff and patients, indicating that the striking difference is not only between carriage in the community, but between carriage and disease isolates in the same setting [14,15]. This difference suggests that an intervention aimed at MRSA in the hospital setting may be sufficient to control this pathogen [21,22].

The strength of our work is that it provides a representative national dataset for AMR infections in over a 5-year period. The weakness of the study is that initial analysis of the raw laboratory data indicated a need for a better standardisation of the methodology. For example, the panel of drugs tested against the bacterial isolates frequently changed, and there were extended periods when the susceptibility to key drugs was not tested. In part this was explained by lack of availability of discs for antimicrobial susceptibility testing [7]. In addition, we did not have data on vancomycin resistance in *S. aureus* and carbapenem resistance in *E. coli*, which is another drawback of this study as carbapenem resistance has been reported to increase in the region [23]. In view of the current attention to quality of care and laboratory standardisation in CV [11] and the goals of the national plan to tackle [9], it appears that further efforts are needed to guarantee a high standard of laboratory practice relative to antimicrobial drug susceptibility testing.

In summary our work provides the first study of the profiles of *S. aureus* and *E. coli* in Cabo Verde. The two bacterial species represent, as in other hospitals worldwide, the majority of clinical isolates (72% of all clinical isolates), and the detection over a -year period of an increase in in both species is of great concern. This is especially worrying as it might jeopardise empirical treatment in a setting where antimicrobial susceptibility testing is not widely available. In addition, these results provide the baseline surveillance data to inform the public health planning and antimicrobial resistance master plan in CV. The data are also suitable to support a clinical and health economic study of the impact of developing the existing central clinical microbiology laboratory services on antibiotic prescribing practice and antibiotic resistance, and may have implications for other low and middle income countries with limited medical microbiology laboratory capacity and stewardship systems.

Funding

The work was funded by a grant from the Academy of Medical Sciences Global Challenges Research Fund Networking Grant Scheme GCRFNG\100338 to IIM and SB and by an IRDF travel grant of the University of Leicester to MRO. MP is supported by the National Institute for Health Research (NIHR Post-Doctoral Fellowship PDF-2015-08-102). The views expressed in this publication are those of the authors and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health.

Ethical Approval

Not applicable.

Declaration of Competing Interest

Authors declare no competing interest with respect to the work performed in the manuscript.

References

[1] Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. Pharm Ther 2015;40:277–283..
[2] Antimicrobial Resistance. In Global Report on surveillance. Geneva, Switzerland: World Health Organization; 2014 WHO.
[3] O'Neill J. The review on antimicrobial resistance tackling drug-resistant infections globally: final report and recommendations. London: Review on antimicrobial resistance; 2016. p. 1–84.
[4] Hernando-Amado S, Coque TM, Baquero F, Martinez JL. Defining and combating antibiotic resistance from one health and global health perspectives. Nat Microbiol 2019;4(9):1432–42.
[5] Nellums LB, et al. Antimicrobial resistance among migrants in Europe: a systematic review and meta-analysis. Lancet Infect Dis 2018;18(7):796–811.
[6] Ginting F, et al. Rethinking antimicrobial resistance surveillance: a role for lot quality assurance sampling. Am J Epidemiol 2019;188(4):734–42.
[7] Barbe B, Yansouni CP, Affolabi D, Jacobs J. Implementation of quality management for clinical bacteriology in low-resource settings. Clin Microbiol Infect 2017;23(7):426–33.
[8] Lourenço J. Epidemiology of the zika virus outbreak in the Cabo Verde islands, West Africa. PLoS Curr 2018 10:ecurrents.outbreaks.19433b1e4d007451c691-f138e1e67e8c.
[9] Ministério da Saúde e Segurança Social e do Ministério da Agricultura e Ambiente da Repu'blica de Cabo Verde. Plano de Ação Nacional de Luta Contra Resistencia Antimicrobiana 2018 - 2022; 1-167; B. O. 34/2018.
[10] Devillard A, Bacchi A, Noack M. A survey on migration policies in West Africa. ICMPD and IOM; 2016.
[11] Correia A, Paula C, Argentina S. Evaluation of the level of implementation of norms and standards for quality of care in health facilities in Santiago island Cape Verde. Antimicrob Resist Infect Control 2013;2(Suppl 1):P337.
[12] Aires-de-Sousa M, Conceição T, De Lencastre H. Unusually high prevalence of nosocomial Panton-Valentine leukocidin-positive *Staphylococcus aureus* isolates in Cape Verde Islands. J Clin Microbiol 2006;44(10):3790–3.
[13] Weinstein Melvin P. CLSI. performance standards for antimicrobial susceptibility testing.. 29th ed. CLSI supplement M100 Wayne, PA: Clinical and Laboratory Standards Institute; 2019.
[14] Conceição T, Coelho C, De Lencastre H, Aires-de-Sousa M. High revalence of biocide resistance determinants in *Staphylococcus aureus* isolates from three African countries. Antimicrob Agents Chemother 2015;60(1):678–81.
[15] Aires-de-Sousa M, Santos Sanches I, Ferro ML, De Lencastre H. Epidemiological study of staphylococcal colonization and cross-infection in two West African Hospitals. Microb Drug Resist 2000;6(2):133–41.
[16] Leopold SJ, van Leth F, Tarekegn H, Schultsz C. Antimicrobial drug resistance among clinically relevant bacterial isolates in sub-Saharan Africa: a systematic review. J Antimicrob Chemother 2014;69(9):2337–53.
[17] Tadesse BT, et al. Antimicrobial resistance in Africa: a systematic review. BMC Infect Dis 2017;17(1):616.
[18] Köck R, et al. Methicillin-resistant *Staphylococcus aureus* (MRSA): burden of disease and control challenges in Europe. Euro Surveill 2010;15(41):19688..
[19] Enright MC, Robinson DA, Randle G, Feil EJ, Grundmann H, Spratt BG. The evolutionary history of methicillin-resistant *Staphylococcus aureus* (MRSA). Proc Natl Acad Sci U S A 2002;99(11):7687–92.
[20] Wertheim HF, et al. Low prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) at hospital admission in the Netherlands: the value of search and destroy and restrictive antibiotic use. J Hosp Infect 2004;56(4):321–5.
[21] Robotham JV, Jenkins DR, Medley GF. Screening strategies in surveillance and control of methicillin-resistant *Staphylococcus aureus* (MRSA). Epidemiol Infect 2007;135(2):328–42.
[22] Robotham JV, Scarff CA, Jenkins DR, Medley GF. Meticillin-resistant *Staphylococcus aureus* (MRSA) in hospitals and the community: model predictions based on the UK situation. J Hosp Infect 2007;65(2):93–9.
[23] Poirel L, Goutines J, Aires-de-Sousa M, Nordmann P. High rate of association of 16S rRNA methylases and carbapenemases in *Enterobacteriaceae* recovered from hospitalized children in Angola. Antimicrob Agents Chemother 2018;62:e00021–18.olume-nr>62:.