Carbapenem-resistant Enterobacteriaceae: global action required

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Enterobacteriaceae are common pathogens in hospitals and in the community. When resistant to powerful and versatile antibiotics such as carbapenems, they can have devastating consequences, particularly in the most vulnerable individuals.[1] Much information about the clinical impact of carbapenem-resistant Enterobacteriaceae (CRE) comes from high-income countries.[2,3] Yet, the brunt of the CRE epidemic is borne by low-income and middle-income countries (LMICs), which must also cope with fragile health-care systems that are often overburdened.

In *The Lancet Infectious Diseases*, Andrew Stewardson and colleagues[4] present the clinical and microbiological characteristics of bloodstream infections caused by CRE in patients from LMICs. The authors organised an international collaboration comprising 16 hospitals from ten LMICs. Up to 20 cases of bloodstream infections caused by CRE and 20 caused by carbapenem-susceptible Enterobacteriaceae (CSE) were included from each hospital. Of 297 patients prospectively enrolled, approximately two-thirds had confirmation of CRE or CSE by antibiotic susceptibility testing, multilocus sequence typing, and molecular detection of relevant carbapenemases. The investigators reported in-hospital mortality in 35 (20%) of 174 patients with CSE bloodstream infection and 43 (35%) of 123 patients with CRE bloodstream infection. CRE bloodstream infection was associated with a 75% increased probability of in-hospital mortality, an almost 40% decreased probability of being discharged alive, and an increased length of hospital stay of 3·7 days.

Stewardson and colleagues are to be commended for their effort to include hospitals in LMICs from various regions. Rather than a comprehensive assessment of CRE in each participating country, or globally, this study provides an interesting snapshot. Readers from the USA will be interested to learn that *Klebsiella pneumoniae* belonging to clonal complex 258 and carrying bla_{KPC} is not the main type of CRE outside of the Americas.[5] Instead, *K pneumoniae* ST14 harboring bla_{NDM} and *K pneumoniae* ST231 carrying $bla_{OXA\text{-}48\text{-}like}$ were predominant in south Asia. *K pneumoniae* ST307, an emerging high-risk clone, was not detected;[6] neither was *K pneumoniae* ST14 nor the virulent serotype K1, perhaps because sites from east Asia were not included.

As clinicians, we do not have clear evidence that differences in patients' outcomes are influenced by genotypic differences in CRE. Nevertheless, understanding the molecular epidemiology of CRE has important diagnostic and therapeutic implications. The error rate in the determination of carbapenem susceptibility by conventional methods at study sites was 8% (17 of 207). However, selecting molecular targets for CRE detection is challenging given the variety of carbapenemases, including 13 (13%) of 100 CRE isolates without a carbapenemase gene. Polymyxins, although active and used against a high proportion of CRE in this study, have poor safety and efficacy; carbapenems were also used to treat the majority of both CSE and CRE bloodstream infections. This finding highlights the need for alternative agents with activity against CRE. Combinations of antibiotics containing avibactam (a β-lactamase inhibitor active against OXA-48 and *K pneumoniae* carbapenemase) or vaborbactam (active against *K pneumoniae* carba-penemase) are available to treat CRE in high-income countries.[7–9] However, these combinations are expensive, and are not effective against CRE harbouring metallo-β-lactamases such as New Delhi metallo-β-lactamase.

International efforts such as the one undertaken by Stewardson and colleagues warn us that CRE is a challenge for both high-income countries and LMICs. Clearly, the underlying characteristics of patients and treatment patterns are not uniform across different locations and times, invalidating comparisons with previously published cohorts of patients with CRE bloodstream infection. And yet, we might be hopeful for progress in improving the outcome of patients with serious infections caused by CRE. We look forward to the results of other international collaborations that are underway, such as CRACKLE II[10] and EURECA.[11]

Inspired by studies such as these, we must ask how we can take global action against CRE. At a minimum, every country should have a national action plan tasked with measuring the prevalence of CRE and other resistant phenotypes, promoting the prudent use of antibiotics

in health care and in animal husbandry, immunising their population, and investing in water sanitation.[12] Additionally, high-income countries should have the responsibility—and interest—to spend the resources necessary to develop and implement better diagnostics that accurately detect CRE, and antibiotics effective against CRE that are also safe and affordable. For these solutions to have a global impact, collaboration among high-income countries and LMICs is essential.

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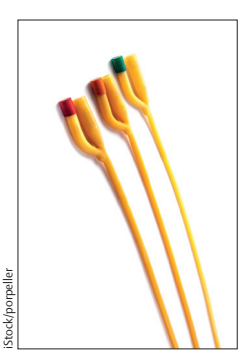
Non-antibiotic prevention strategies against catheter-associated urinary tract infections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Health-care-associated infections are an important cause of morbidity, mortality, and prolonged hospital stay among inpatients, which result in substantial costs. Prevalence of health-care-associated infections among inpatients varies between 3·2% in the USA, 7·1% in Europe, and 15·5% in developing countries.[1–3] Catheter-associated urinary tract infection (UTI) is one of the most common health-care-associated infections. Yet, a substantial proportion of health-care-associated infections, especially catheter-associated UTIs (with a prevalence of 65–70%), are preventable[4]. It seems that the lower prevalence of health-care-associated infections in the USA than in Europe and in developing countries is mainly due to the reduction in the prevalence of catheter-associated UTIs and surgical-site infections through the implementation of national prevention programmes.[1] Therefore, prevention strategies for health-care-associated infections are essential; particularly, effective non-antibiotic strategies are urgently needed, since the prevalence of antimicrobial resistance is increasing and antibiotic consumption is its main driving force.[5,6]

In the *The Lancet Infectious Diseases*, Oyebola Fasugba and colleagues[7] studied the efficacy of 0·1% chlorhexidine solution for cleaning the urethral meatus before urinary catheterisation, a good example of a non-antibiotic prevention method. In a cross-sectional, stepped-wedge, open-label, randomised study, the authors showed that meatal cleaning with chlorhexidine (intervention population) before catheter insertion was superior to normal saline cleaning (control population) for the prevention of catheter-associated asymptomatic bacteriuria and UTI