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Editorial

The global challenge of carbapenemases and the critical need for more data

Verona Integron-encoded Metallo-β-lactamase (VIM), which was initially described in Italy in 1997, and has disseminated globally (Nordmann et al., 2011). In the current study, Moubareck et al. described a high prevalence of carbapenem non-susceptible *Pseudomonas aeruginosa* (23.9%) from a survey of 1969 human isolates from four hospital in Dubai, of which only 37 isolates were available for further PCR testing.

Of the 37 isolates, PCR tested from two out of four study hospitals, 12 (32.4%) were positive for the VIM carbapenemase gene. Clinical data on the subjects were also largely not available. This is unfortunate as much more information could have been gleaned from a more comprehensive analysis from all the representative hospitals.

Carbapenemases are an emerging problem not just in *Enterobacteriaceae* but also in *Pseudomonas*. Outbreaks of carbapenemase-producing *Pseudomonas* have been reported in Asia (Molton et al., 2013), but not to date from the middle east.

This report has some very interesting molecular epidemiological data suggesting clonal spread of carbapenemase-producing *Pseudomonas* in at least two healthcare facilities in Dubai. Such data are invaluable and need to be correlated with international data documenting the emergence of "high-risk clones" of metallo-betalactamases in *Pseudomonas* (Wright et al., 2015). Whole genome sequencing (WGS) is rapidly becoming the gold standard for molecular epidemiology in high-income countries with resources comparable to the United Arab Emirates. WGS is clearly within the capability of investigators in the region as demonstrated by Moubareck et al. and more data from the region would help us better understand the global spread of resistant clones especially in large cosmopolitan trading hubs such as Dubai. At the local level, WGS data can also inform infection control and prevention strategies (Khong et al., 2016).

Molecular epidemiology cannot function in isolation and needs to be correlated with "shoe leather" epidemiology to clarify modes of transmission, risk factors for acquisition and the effectiveness of control strategies. It is unfortunate that clinical data were not available for the patients from whom the isolates were obtained for the molecular analysis. While there is often initial resistance to doing detailed epidemiological analyses including careful prospective studies with appropriate controls or quasi-experimental studies assessing the impact of various infection control interventions, countries with high levels of medical care have an even greater need and obligation to provide correspondingly high levels of infection prevention and control. These can only function effectively with inter-institution and intra-institution collaborative analyses and epidemiological studies.

This important study provides much-needed information on carbapenemase molecular epidemiology in the Gulf Cooperation Council (GCC) states (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and the United Arab Emirates), a region of mostly high-income countries currently lacking in antimicrobial resistance surveillance data. Limited studies reveal widespread occurrence of carbapenemase-producing Gram-negatives in the GCC states (Al-Baloushi et al., 2018; Zowawi et al., 2018).

However, there is to our knowledge, no published systematic surveillance data available from the GCC countries detailing the prevalence of carbapenemase-producing Gram-negatives. Furthermore, there are no large multi-centred studies describing the clinical impact and outcomes of these organisms in the GCC region. There are several large international collaborative studies ranging from the early SENTRY and MYSTIC studies which encompassed dozens of countries across the globe but few in the Middle East. Currently, there are a number of ongoing collaborative networks including PANORAMA (Stewardson et al., 2019), the ARLG (Chambers et al., 2014), the Global PPS study (Versporten et al., 2018), the INICC (Rosenthal, 2016) and others. These networks provide varying levels of resources but more importantly standardized case definitions and also laboratory protocols which enable a better understanding of these important pathogens.

The GCC countries could benefit significantly from active participation and even leadership in these global networks. They would not only improve patient care for residents of these countries, but they could also help to raise the standards of middle- and even low-income countries in the surrounding eastern Mediterranean region or the broader middle east and north Africa.

Overall, however, the authors should be commended for putting together an analysis of a subgroup of patients from a large cohort with carbapenem resistance in Pseudomonas. The GCC states, like other high-income countries, are seeing more and more use of high technology surgical techniques as well as immunosuppressive therapies in oncology and transplant. It is vital that epidemiological surveillance for antimicrobial resistance keeps pace with technological developments in other areas of clinical medicine and surgery otherwise, many of the gains of medicine of the last few decades will be lost as we look to the spectre of returning to the "pre-antibiotic era" for many of our most vulnerable patients. This is a global problem that affects low- and middle-income countries disproportionately. The high-

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income countries in the GCC have the opportunity to make a huge difference in our understanding of the spread of resistant pathogens beyond the usual places where good data exist in Europe, North America and parts of South and East Asia. We hope that this will be the first of many manuscripts with more comprehensive data to lay the groundwork for a scientific approach to the problem of antimicrobial resistance in the middle east and beyond.

We encourage private and public hospitals in the region to collaborate in surveillance of hospital infections by sharing data and especially by exchanging isolates of MDR and XDR bacteria.

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