**Title**

The State of ESKAPE in Malaysia

**Authors**

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**Letter**

Sir,

*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species are together responsible for a significant global disease burden for which the acronym ‘ESKAPE’ was devised to discuss them collectively. Much of their associated morbidity and mortality is due to nosocomial emergence of antimicrobial resistance (AMR) in ESKAPE organisms, which enables the pathogen to escape the bactericidal actions of formerly effective antibiotic treatments. Unnecessary prescribing and inappropriate use of antibiotics has accelerated the evolution of AMR, to the point that it is now a persistent problem [1]. Until recently, AMR was predominantly reported in high-income countries [2]. However, ESKAPE emergence, extent, and causes of resistance in low and middle-income countries needs also to be monitored to help tackle AMR globally.

To reduce the human and economic costs associated with AMR infections in the healthcare environment, high quality surveillance is a fast-growing and evolving field around the world [3]. Issues of laboratory capacity still widely limits AMR surveillance around the world however. Nonetheless, appropriate action can help inform infection control measures for a safer clinical environment and guide prescribing to optimise patient treatment. As such, Malaysia produces a National Surveillance of Antibiotic Resistance (NSAR) report, to provide annual data on the antibiotic sensitivities of bacteria isolatedfrom patients, including ESKAPE organisms. Since the Institute of Medical Research began publishing the NSAR report in 2007, participation has grown from just 12 hospitals to 39 hospitals in 2014. This has improved the geographical coverage of AMR reported, with data from each of the thirteen states, as well as Federal Territories of Kuala Lumpur and Putrajaya.

Comparison of AMR prevalence amongst the ESKAPE pathogens in the most recently available NSAR report [4] reveals that the proportion of resistance to the antibiotics tested has largely remained the same or declined slightly compared with 2013 figures [5]. The proportion of *S. aureus* isolates resistant to methicillin fell marginally, and percentages of methicillin resistant *S. aureus* isolates resistant to the other eight agents tested declined or barely changed, except for ciprofloxacin where the percentage resistant increased somewhat. Among Gram-negative ESKAPE pathogens, there was generally little change in resistance to the eight antibiotics tested, although there were some notable exceptions. Firstly, resistance to piperacillin/tazobactam increased from 51.6% to 55.4% among *Acinetobacter spp*. between 2013 and 2014. Secondly, the percentage of cefoperazone/sulbactam resistant isolates fell dramatically from 41% to 25.7% over one year. Between 2013 and 2014, increased percentages of ampicillin/sulbactam resistant *E. coli*, cefepime and cefoperazone/sulbactamresistant *K. pneumoniae*, and cefotaxime and ceftazidime resistant *Enterobacter cloacae* were also noted.

High quality infection surveillance and analysis of associated AMR enables prevalence trends to be identified to help guide antibiotic prescribing, infection control practices and alert health authorities to the emergence of new or unusual resistant strains on an institutional, right up to the global, level [3]. Here, the data and analysis in the publicly available NSAR report could be improved. The report does not detail the criteria for inclusion of isolates, distinguish between infection and colonisation, nor report whether isolates originated from hospital or community acquired infections. Additionally, resistance is not reported as a rate. It is thus unclear whether changes in the number of isolates tested reflects variation in patient number, fluctuating incidence of infection or simply inconsistent participation in the programme. Whether individual hospitals use the statistics they contribute to the NSAR data pool to inform infection control measures towards reducing infection rates on a local level, is unknown. Year-on-year analysis of the surveillance data collated would be more useful in identifying potentially significant trends in AMR, than the present simple comparison with the preceding year. Further value could be gained from the NSAR report if multiple drug resistance among isolates was investigated to guide appropriate antibiotic prescribing - cheaper, clinically beneficial to the patient, and a means to reduce consumption of unnecessary antibiotics which accelerates AMR development.

The evolution of AMR in pathogens is relentless against a backdrop of global healthcare systems increasingly burdened by population growth, ageing populations and increasing numbers of immunocompromised patients. Modern hospitals are proving a powerful selective environment for AMR, particularly amongst the ESKAPE pathogens. The threat from AMR is compounded by the phenomenon of multiple drug resistance. Improvements in infection control practice, better antibiotic stewardship and research and development into new antibiotics will help resist the constant spread of AMR pathogens, but needs the guidance of data from local healthcare surveillance, to ultimately feed into global programs. The activities of the Institute of Medical Research in Malaysia highlights the deficiencies in effective surveillance in a developing economy in South East Asia. Never has the need for local healthcare surveillance with cooperation on a global scale been needed more, placing it in a critical position in the quest to control the spread of AMR.

**References**

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