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Short report

Point-prevalence survey of carbapenemase-producing Enterobacteriaceae and vancomycin-resistant enterococci in adult inpatients in a university teaching hospital in the UK

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SUMMARY

Infections with carbapenemase-producing Enterobacteriaceae (CPE) and vancomycin-resistant enterococci (VRE) are associated with increased morbidity and mortality, but the carriage rates of CRE and VRE among hospital inpatients are unknown. A point-prevalence survey was conducted to determine CPE and VRE carriage rates in hospitalized adults. Eight hundred and eighteen of 960 (85.2%) adult inpatients were invited to participate in the study. Of these, 595 patients (72.7%) consented and provided specimens. Of 540 samples tested, none were positive for CPE. One hundred and thirty of 540 (24.1%) samples were VRE positive, and 34 of 40 (85%) of wards had cases. Universal screening for CPE may not be cost-effective in low-prevalence settings, but targeted screening of high-risk patients should continue. The optimal screening strategy for VRE remains to be determined, as universal screening and isolation is not feasible in the study setting.

Introduction

The rising incidence of multi-drug-resistant organisms such as carbapenemase-producing Enterobacteriaceae (CPE) is a global public health emergency that threatens the advances made by modern medicine over the past century. Infections with CPE result in increased mortality [1], and Public Health England (PHE) Antimicrobial Resistance and Healthcare Associated Infections Reference Laboratory is reporting increasing numbers of CPE isolates [2]. Routine screening for CPE is not recommended in the UK, where national screening guidelines advise a risk-based approach [3]. The true prevalence of CPE carriage and infection amongst hospital inpatients remains unknown.

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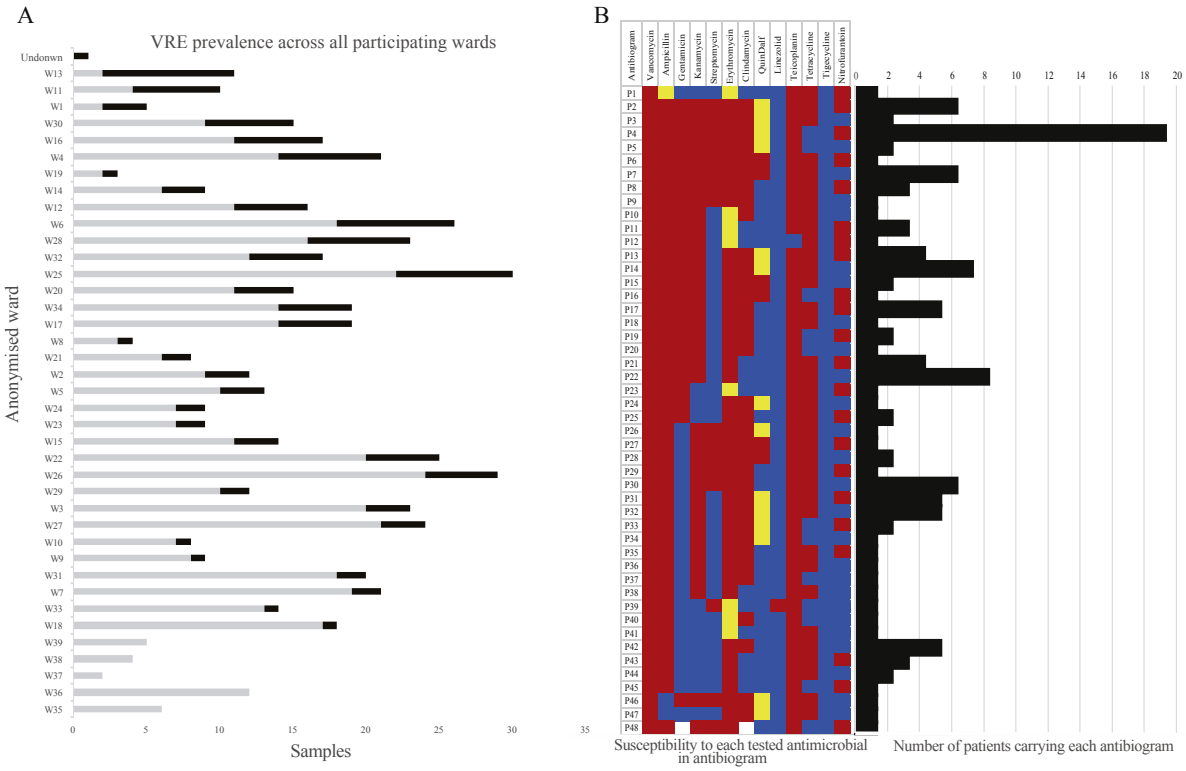

Figure 1. Prevalence and antibiotic susceptibility patterns of vancomycin-resistant enterococci (VRE) isolates. (A) Bar chart demonstrating the number of samples positive (black) and negative (grey) for VRE for each ward (W) within the hospital. (B) Heat map demonstrating the different antimicrobial susceptibility profiles (P1–P48) of the VRE isolates. Red indicates non-susceptibility to the antibiotic tested, yellow indicates intermediate susceptibility to the antibiotic tested, blue indicates susceptibility to the antibiotic tested, and white indicates no data available. The bar chart to the right of the antibiograms shows the number of patients positive for each antibiogram within the VRE positive isolates. QuinDalf, quinupristin-dalfopristin.

Infections caused by vancomycin-resistant enterococci (VRE) are also associated with increased morbidity, mortality, healthcare costs and duration of hospital stay compared with infections caused by vancomycin-susceptible enterococci [4]. VRE bloodstream infections in England were previously subject to mandatory reporting, but this was changed to voluntary reporting in April 2013. The prevalence of VRE carriage in hospital inpatients remains unknown.

The authors previously conducted a six-month prospective surveillance study of multi-drug-resistant organisms, including CPE and VRE, in all patients admitted to the adult intensive care unit from June to December 2016. An unsuspected outbreak of *Klebsiella pneumoniae* carrying the New-Delhi metallo-beta-lactamase gene bla_{NDM-1} was detected. This outbreak spread to several wards before it was controlled in July 2016, prior to its re-emergence five months later. Asymptomatic VRE carriage was also detected in almost 25% of adults admitted to the intensive care unit during the study period. In order to investigate potential reservoirs of CPE and VRE in the study hospital, a point-prevalence survey of all adult inpatients was conducted in June 2017.

Methods

The infection control team organized screening of all adult inpatients aged ≥18 years during a three-day period in June 2017. Each patient was asked to provide a rectal swab or a stool sample, and was asked questions about risk factors for CPE, based on those described in the PHE CPE screening toolkit [3]. Patients were asked if they had been hospitalized in the UK in the previous 12 months. If they had, patients were asked if this had been in London or Manchester (i.e. areas with high prevalence of CPE). Patients were also asked if they had been hospitalized abroad in the previous 12 months, and if so, in which country. Finally, patients were asked if they recalled being asked the screening questions before, and if they had been screened for CPE previously. The emergency department, day care wards and paediatric wards were excluded from the study. Moribund patients and those who were unable to provide consent for themselves were not approached for participation in the study. Patients were informed about the survey and provided verbal consent for participation. Ethical approval was not required as the study was conducted under the auspices of surveillance for healthcare-associated infections. All patient data and sample data were linked and anonymized prior to analysis.

Rectal swabs were collected using Sigma Transwabs (MWE, Devizes, UK), and stool samples were collected into standard specimen containers. Samples were delivered to the research laboratory on the day of collection and processed within 24 h by inoculating directly on to CARBA Smart agar (bioMérieux, Marcy-l'Étoile, France) and Brilliance VRE agar (Oxoid, Basingstoke, UK) prior to incubation at 37ºC for 24–48 h. Potential CPE isolates were confirmed using the Xpert Carba-R

Table I
Medical/surgical specialities of patients positive for vancomycin-resistant enterococci

Speciality	Number of patients
Acute medicine	9
Cardiology	3
Clinical oncology	3
Colorectal surgery	6
Critical care medicine	1
Diabetic medicine	4
Ear, nose and throat	1
Gastroenterology	3
General medicine	4
General surgery	2
Geriatric medicine	11
Haematological oncology	4
Haematology	9
Hepatology	3
Hepatobiliary and pancreatic surgery	8
Infectious diseases	1
Intestinal failure	1
Transplant surgery	5
Medical oncology	2
Nephrology	7
Neurology	2
Neurosurgery	6
Orthopaedics	6
Plastic surgery	1
Renal transplant follow-up	1
Small bowel assessment	1
Stroke medicine	6
Thoracic medicine	7
Trauma	3
Unknown	1
Upper gastrointestinal surgery	3
Urology	1
Vascular surgery	5

assay (Cepheid, Sunnyvale, CA, USA). Species identification was confirmed using matrix-assisted laser desorption ionization–time of flight mass spectrometry (Bruker, Billerica, MA, USA). Antimicrobial susceptibility testing was performed using Vitek-2 (bioMérieux).

Results

According to the hospital information system, 954 patients admitted to 42 wards were eligible to participate in the study. One hundred and thirty-six patients were not approached and the reason for this was not documented. Of the remaining 818 patients, 595 (72.7%) provided verbal consent and specimens. The reasons for samples not being collected were as follows: 132 of 818 (16.1%) declined consent, 57 of 818 (7%) were unable to consent, 11 of 818 (1.3%) were unavailable (e.g. because they were undergoing a medical procedure), and the reason was unknown in four of 818 (0.5%) cases. Nineteen patients (2.3%) were excluded because they were sampled more than once (N=18) or because they were aged under 18 years (N=1). In total, only 18 of 595 (3%) samples were unaccounted for.

Data regarding risk factors for CPE were obtained from 509 of 595 (85.5%) study participants. In terms of risk factors for CPE, 318 of 509 (62.5%) patients had attended a UK hospital in the previous 12 months, 179 of 509 (35.2%) patients had been admitted to the study hospital previously, four of 509 (0.78%) patients had been admitted to a London hospital, and three of 509 (0.6%) patients had been hospitalized abroad. No patients had been admitted to a hospital in North West England. Interestingly, despite high rates of prior hospital admission in the study population, only 28 of 509 (5.5%) participants could recall having been asked questions previously about risk factors for CPE.

Of the 577 samples tested, none were positive for CPE. Thirty-seven samples were tested for CPE alone, and 140 of 540 samples (25.9%) grew colonies suggestive of enterococci on the VRE-selective media. Eight of these isolates failed to grow on subculture, and two were identified as vancomycin-susceptible *Enterococcus faecalis* and excluded from the analysis. Thus, 130 of 540 (24.1%) samples were positive for vancomycin-resistant *E. faecium* [median carriage rate per ward N=3, range 0–9 patients, interquartile range 3–5 patients]. Carriage of VRE was detected in the majority of wards tested, with only five of 39 (12.8%) wards having no VRE cases; two wards tested patients for CPE alone (Figure 1A). VRE carriage was detected in more than 50% of screened patients in three wards (Ward 1, three of five patients, 60%; Ward 11, six of 10 patients, 60%; Ward 13, nine of 11 patients, 82%) and in 33 different patient specialities. Specific details of the types of patient or their medical condition(s) were not collected, but the specialities of VRE-positive patients are indicated in Table I.

Differences in antimicrobial susceptibility profiles (antibiograms) of organisms such as meticillin-resistant *Staphylococcus aureus* are often used as a surrogate marker for transmission between patients by infection control practitioners [5]. This approach was applied to the VRE isolates in the study in order to examine potential transmission events between asymptomatic patients. Forty-eight different antibiograms (median 1, range 1–19, IQR 1–3) were identified among the 130 isolates. The most frequently identified antibiogram was antibiogram 4 (19 patients) (Figure 1B).

Discussion

This survey suggests that CPE prevalence in this adult inpatient population is low, and that the previous outbreaks were related to spread from a point source, rather than widespread carriage. The findings concur with the low carriage rates reported previously by Otter *et al.* [6]. This is reassuring in that it suggests that the hospital does not have a reservoir of unidentified CPE. However, routine screening of high-risk patients, such as those in intensive care, may be beneficial in detecting colonized patients at an early stage, before they cause clinical infections or outbreaks. This would enable proactive action to reduce transmission and spread among vulnerable patients. This study identified seven patients who had come from 'high-risk' areas for CPE, such as London or overseas, but no patients from North West England. Most of the patients identified with CPE had no recognized risk factors, and had only been admitted to the study hospital previously, rather than elsewhere. A concerning finding was the low level of

patient recall of CPE screening questions. All patients should have been asked these questions on admission in order to identify high-risk patients and isolate them pending the screening results. Whilst this may have been confounded by patients' abilities to recall questioning, it also suggests that the CPE screening toolkit may not be being implemented correctly.

In contrast, high rates of asymptomatic carriage of VRE were detected, similar to those reported in a previous study based in Ireland [7]. VRE is known to be associated with higher morbidity, mortality and length of stay, despite the availability of effective treatment [4]. VRE have been identified frequently as causative agents of outbreaks and transmission in vulnerable patient groups, particularly in highly immunocompromised patients (e.g. those with haematological malignancies) [8]. Antibiograms have been used previously to investigate transmission of nosocomial pathogens [5]. Asymptomatic colonization of patients, particularly those who are immunocompromised, risks unseen transmission to other patient groups. VRE colonization has been shown to precede infection in hospital patients [9], and an association between duration of antibiotic therapy and increased risk of VRE bacteraemia has been reported recently [10]. Whole-genome sequencing (WGS) has demonstrated that antimicrobial susceptibility profiles lack accuracy in determining transmission and relatedness of lineages for VRE [11]. The present authors are planning WGS analysis of this dataset to provide further insight into the population structure of VRE and potential transmission events within the study hospital.

Strategies to reduce VRE in patients including screening, isolation and implementing contact precautions in VRE-positive patients have shown variable success [12,13]. In the study setting, isolation of all patients positive for VRE carriage would be impossible due to an insufficient number of side rooms and isolation facilities; this issue is likely to be common in many hospitals in the UK and elsewhere. Cohorting of positive patients may be an option, but this is often implemented in the context of infection control 'bundles', so direct efficacy is difficult to determine [14—16]. The logistics of large-scale cohorting and infection control bundles may have an adverse impact on patient care, time management, staffing levels, bed numbers and overall costs to hospitals [17,18]. In this instance, a risk-based approach to screening and isolation may be a suitable compromise. Those patients considered to be at high risk of VRE, such as transplant or oncology patients, may benefit from enhanced contact precautions, guided by the results of targeted screening.

Although the failure to detect CPE carriage in adult inpatients in this survey was reassuring, several limitations of this study are acknowledged. Firstly, only 72.7% (595 of 818) of eligible adult inpatients participated in the survey. Secondly, patients attending the emergency department, day cases, children or moribund patients were not sampled. Therefore, CPE and VRE carriage may have been missed in these patient populations. Thirdly, there may have been variation in sample collection technique, as samples were collected by many different staff members on the different wards. Finally, broth enrichment was not performed prior to plating samples on to selective media, which may have reduced the sensitivity of detection. Despite these caveats, this study provides important new information on the prevalence of CPE and VRE in adult inpatients at a large UK teaching hospital.

In conclusion, a point-prevalence survey for CPE and VRE carriage in adult inpatients was performed in June 2017. Reassuringly, CPE carriage was not detected in this population on this occasion, despite the limitations outlined above. However, high rates of VRE carriage were found, and this appeared to be spread throughout the hospital. These findings suggest that universal screening for CPE may not be cost-effective in low-prevalence settings, but targeted screening of high-risk patients should continue to be implemented. Given the high prevalence of VRE carriage in the study hospital, the optimal strategy for screening and management of VRE remains to be determined, as universal screening and isolation of all patients is not feasible in this setting.

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Conflict of interest statement
None declared.

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