Point prevalence survey of carbapenemase-producing Enterobacteriaciae (CPE) and vancomycin-resistant *Enterococci* (VRE) in adult inpatients in a University teaching hospital in the United Kingdom

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Introduction

Antimicrobial resistance is a global public-health emergency, which threatens the advances made by modern medical care over the past century. The World Health Organisation has recently published a global priority list of antibiotic-resistant bacteria, which includes carbapenemase-producing *Enterobacteriaceae* (CPE) and vancomycin-resistant *Enterococci* (VRE). Infections with CPE result in increased mortality and there are reports of increasing numbers of CPE isolates. Infections caused by VRE are also associated with increased morbidity, mortality, healthcare costs and durations of hospital stay.

We have previously conducted a six-month prospective surveillance study for Multi-Drug Resistant Organisms (MDRO) in the adult Intensive Care Unit at Addenbrooke's Hospital. We detected two separate outbreaks of *Klebsiella pneumoniae* carrying the New-Delhi metallo-beta-lactamase gene bla_{NDM-1}. This outbreak spread to several wards before it was controlled, prior to its re-emergence five months later. Asymptomatic VRE carriage was also detected in almost 25% of adults. In order to investigate potential reservoirs of CPE and VRE in our hospital, we conducted a point prevalence survey of all adult inpatients in June 2017.

Methods

We conducted a three-day point prevalence survey in June 2017 to determine CPE and VRE carriage rate among adult inpatients in our hospital. All adult inpatients (aged ≥18 years) were eligible for inclusion in the study. The Infection Control team and ward nurses explained the study, obtained verbal consent from participants and enrolled patients into the study.

A single rectal swab or stool sample was collected for each enrolled patient using Sigma Transwabs (MWE, Wiltshire, England) or standard specimen containers. Samples were delivered to the research laboratory and processed within 24 hours of receipt. Samples were plated onto selective chromogenic media - CHROMID CARBA SMART (bioMerieux, Marcy l'Etoile, France) and Brilliance VRE (Oxoid, Basingstoke, UK) – and incubated at 37˚ C for 24-48 hours. Suspect colonies were sub-cultured onto Columbia Blood Agar (Oxoid, Basingstoke, UK) with either a meropenem antibiotic disc for CPE, or vancomycin for VRE isolates. Resistant isolates were identified using matrix-assistant laser desorption/ionisation-time of flight mass spectrometry (MALDI-TOF). Samples that were identified as CPE or VRE underwent antimicrobial susceptibility testing using the Vitek-2 platform – N350 card for Gram-negative isolates and P607 card for VRE (bioMérieux, Marcy l'Etoile, France). Carbapenem-resistant isolates were tested for carbapenamase genes using the Xpert Carba-R assay (Cepheid, California, United States).

Results

954 patients admitted to 42 wards were eligible for inclusion in this study. 818 / 954 (85.7%) patients were approached and 595 / 818 (72.7%) provided verbal consent and samples.

A total of 577 samples were processed and analysed (18 samples unaccounted for). Of the 577 samples processed, none were positive for CPE, and 37 were tested for CPE only.

140 / 540 samples grew colonies suggestive of enterococci on VRE selective media. Eight samples failed to grow on subculture, and two were identified as vancomcyin-sensitive *Enterococcus faecalis*. 130 / 540 (24.1%) samples were positive for vancomycin-resistant *Enterococcus faecium*. All but five hospital wards (34 / 39, 87.2%) that participated in this study had at least one VRE positive sample identified.

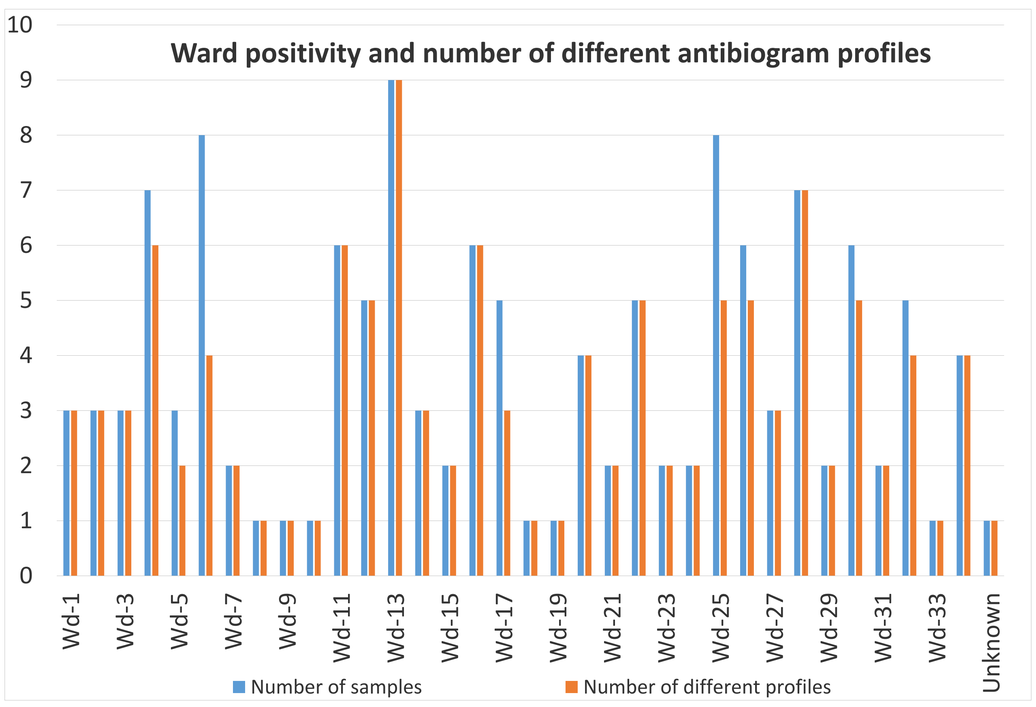

Figure 1. Bar chart showing the breakdown of different wards with number of positive VRE samples, and number of different antibiogram profiles.

Information regarding CPE risk factors was obtained from 509 / 595 patients:

- 318 / 509 (62.5%) patients had attended a UK hospital in the past 12 months
- 179 / 509 (35.2%) patients had been previously admitted to our hospital
- 4 / 509 (0.8%) patients had been previously admitted to a London hospital
- 3 / 509 (0.6%) patients had been hospitalised abroad.

Enterococcal isolates were tested against the following antibiotics: Vancomycin; Ampicillin; Gentamicin; Kanamycin; Streptomycin; Erythromycin; Clindamycin; Quinuprisitin / Dalfopristin; Linezolid; Teicoplanin; Tetracycline; Tigecycline and Nitrofurantoin to generate an antibiotic susceptibility profile (antibiogram).

48 different antibiograms were identified (Figure 2)

- Profile 4 was the most common, identified in 19 patients across 13 wards
- Profile 6, found in one patient, was the most resistant and susceptible to linezolid and tigecycline only
- Profile 39 was the only linezolid resistant sample
- Profile 12 was the only teicoplanin sensitive isolate.

All isolates have been sent for whole-genome sequencing and genotypic results are awaited.

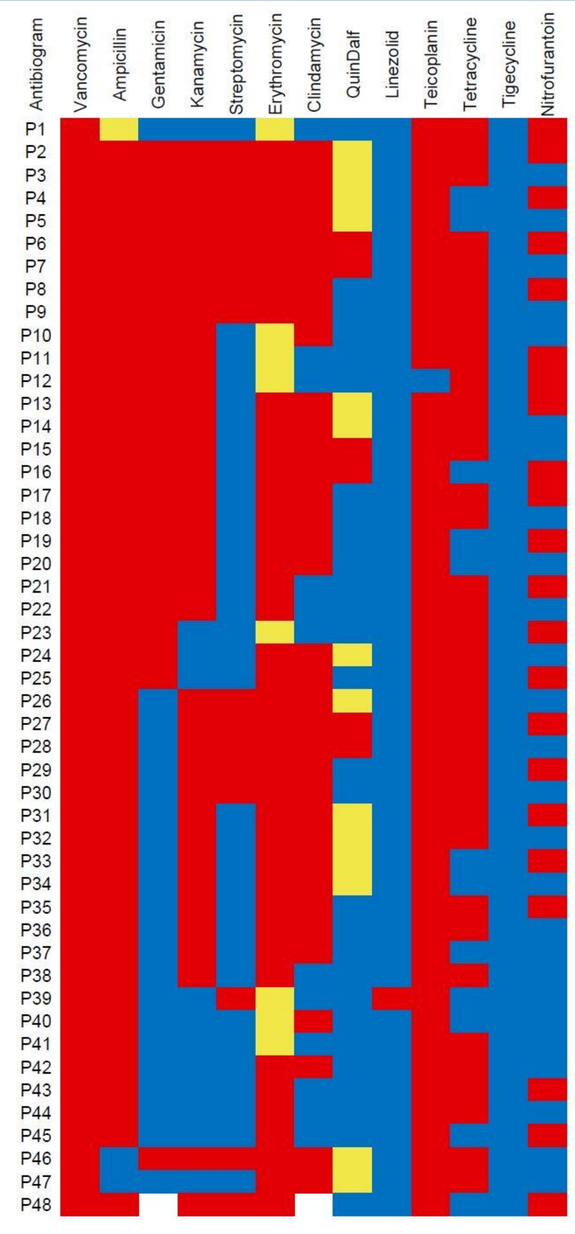

Fig 2. Heat map showing the different antimicrobial susceptibility profiles (P1 to P48) of VRE isolates. Red indicates non-susceptibility, yellow indicates intermediate susceptibility, blue indicates susceptibility, and white indicates no data available.

Conclusions

We performed a point-prevalence survey for CPE and VRE carriage in adult inpatients in our hospital in June 2017. Reassuringly, we did not detect CPE carriage. In contrast, we found high rates of VRE carriage, which appeared to have spread throughout the hospital. We are planning WGS analysis of this dataset to provide further insight into the population structure of VRE and potential transmission events within our hospital.

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