Prospective surveillance and rapid whole genome sequencing detects an unsuspected outbreak of carbapenemase-producing * Klebsiella pneumoniae* in a UK hospital

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**Introduction**

Enterobacteriaceae such as *Klebsiella pneumoniae*, are a major cause of healthcare-associated infections. Antimicrobial resistance caused by carbapenemase-producing Enterobacteriaceae (CPE) is increasing globally, and treatment options are very limited. The prevalence of CPE in UK intensive care units is unknown, as national screening guidelines only recommend screening in patients considered to be at high risk of CPE. Therefore, we conducted a surveillance study for multidrug-resistant (MDR) organisms in the intensive care unit (ICU) using whole-genome sequencing.

**Methodology**

We conducted a surveillance study to determine the prevalence of MDR organisms in an adult ICU. All patients admitted to the ICU during the study period (June – December 2016) were enrolled in the study and screened for MDR O. pneumoniae on admission, on discharge, and weekly during the ICU stay. Surveillance samples included rectal swabs or stool, urine, sputum or tracheal aspirates and wound swabs. Isolates were characterised taxonomically and for their antibacterial susceptibility profiles, before undergoing whole-genome sequencing, to determine the relatedness of the isolates. Environmental samples were collected monthly from the ICU and ward B (involved in the second outbreak), from patient bed bays and fixed and mobile computer stations.

**Results**

- During the first month of the study one participant (ICU006) had a rectal swab positive for an MDR *K. pneumoniae*, which was highly resistant to carbapenem antibiotics but susceptible to colistin.
- Screening and epidemiological investigation identified a further five patients, with epidemiological links to the index case, who were carrying or infected with a multidrug-resistant *K. pneumoniae* strain (Figure 1).
- Five months after the last case, two additional patients on the ICU tested positive for multi-drug resistant *K. pneumoniae*.
- Contact tracing indicated involvement of an additional ward (ward B) and screening of these patients identified two further carriers of the MDR *K. pneumoniae* suggesting reappearance of the outbreak strain.

**Figure 1:** Epidemiological timeline of patients carrying or infected with NDM-1 positive *K. pneumoniae*. Patients are detailed on the vertical axis and time along the horizontal axis. Coloured blocks show stays on different wards by each patient. Vertical/lighter boxes indicate possible contacts between patients on wards. Filled red circles indicate positive infection samples. White circles with red outlines indicate positive carriage samples.

**Results continued**

- Pairwise SNP comparison of suspected outbreak isolates revealed highly related isolates suggesting recent transmission (Figure 3, grey shaded areas).
- Isolates from both outbreaks differed from each other by up to 9 SNPs.
- The isolate from the ‘index’ patient was identical to that of the second patient involved in the outbreak.
- Three environmental isolates from ward B were identical to 2 isolates from patients in the December outbreak.
- Contemporary non-outbreak isolates differed to outbreak isolates by a minimum of 21000 SNPs.
- Outbreak isolates carried more antimicrobial resistance genes (20-24) than non-outbreak ESBL isolates (2-19).
- Other closely related isolates indicated by dark blue areas in Figure 3 were longitudinal isolates collected from the same patient.
- In particular, one patient carried the same lineage in their stool, urine and sputum.

**Conclusions**

- Prospective surveillance of ICU patients identified two unsuspected outbreaks *K. pneumoniae* carrying blaNDM-1, in patients with no risk factors for CPE.
- The outbreak isolates were not closely related to other hospital isolates, suggesting a recent introduction of this lineage.
- We suggest that surveillance for CPE should be extended to all patients in critical care settings.

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