A cluster of carbapenemase-producing hypervirulent *Klebsiella pneumoniae* sequence type 23 in the South-East, Ireland

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Introduction

Classic *Klebsiella pneumoniae* (cKp) is a well-recognised important opportunistic pathogen, associated with nosocomial infections in immunocompromised patients or patients with significant comorbidities. In recent decades, hypervirulent *K. pneumoniae* (hvKp) has emerged, capable of causing community-onset invasive infections in otherwise healthy individuals[1]. hvKp is most associated with pyogenic liver abscesses and has a tendency towards metastatic spread. Reported disseminated infections include empyema, endophthalmitis, meningitis and brain abscesses[1]. hvKp strains were initially reported in East Asia, however global spread has now been documented[2].

While cKp is well-recognised for its ability to acquire antimicrobial resistance determinants, hvKp has largely been susceptible to most antimicrobials[1]. However, reports have emerged of increasing antimicrobial resistance in hvKp strains, including the emergence of carbapenemase-producing hvKp strains[1-4].

The convergence of hypervirulence and antibiotic resistance determinants poses an increasing challenge in the management of these invasive infections. In this report, we describe a cluster of carbapenemase-producing hvKP isolates in the South-East of Ireland over a two-year time period.

Methods

- The microbiology laboratory in University Hospital Waterford (UHW) provides a centralised service for four acute hospitals in the South-East (approx. 1100 beds; population approx. 500,000).
- A retrospective review of new carbapenemase-producing Enterobacterales isolated in the UHW microbiology laboratory from January 2019 to January 2021 was conducted to identify carbapenemase-producing *K. pneumoniae* isolates exhibiting a hypervirulent genotype.
- The isolates exhibiting a hypervirulent genotype were identified by whole genome sequencing (WGS), carried out in the National Carbapenemase-Producing Enterobacterales (CPE) Reference Laboratory.
- Isolates were defined as community-acquired (CA) or hospital-acquired (HA) using the ECDC definitions[5].
- The epidemiological, clinical, and microbiological characteristics of these isolates were reviewed.

Results

- **Twenty-five carbapenemase-producing hvKp isolates were detected, from twenty-two patients over the two-year period.**

Microbiological characteristics:

- All twenty-five isolates were identified by WGS as sequence type 23 (ST23), the most prevalent ST associated with hypervirulence worldwide (see fig. 1).
- All twenty-five isolates were OXA-48 carbapenemase producers.

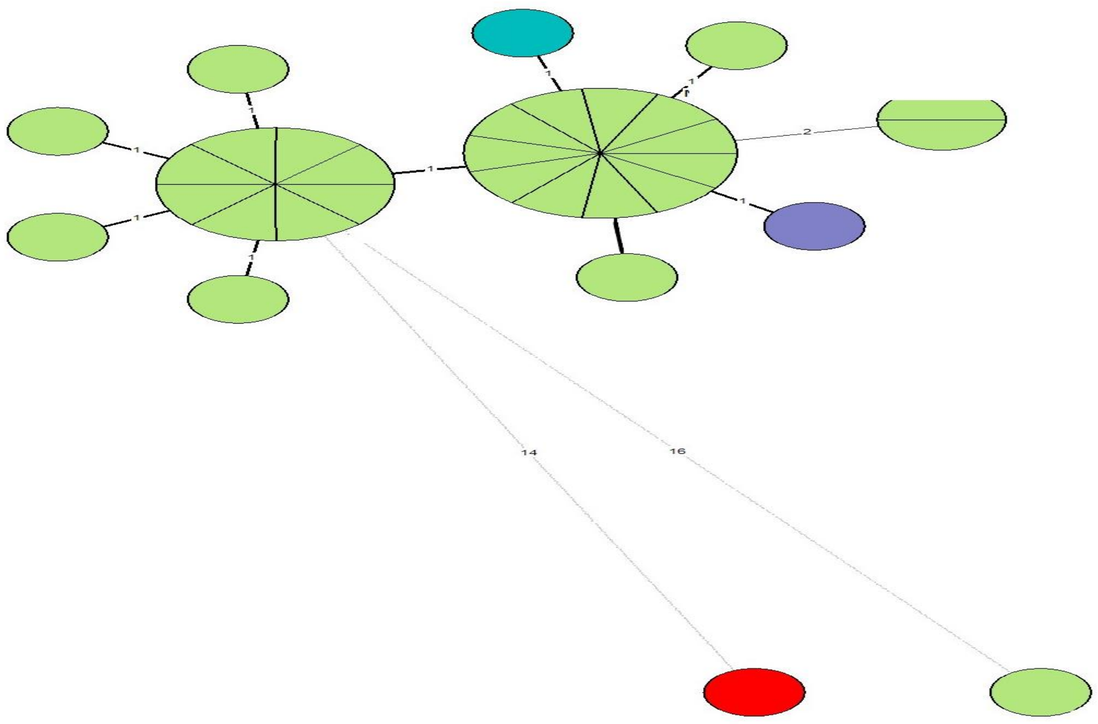

Figure 1. core genome (cg)MLST of *K.pneumoniae* ST23 from the national CPE reference laboratory. All bar three of the isolates are from UHW. All bar two are highly related (clonal group).
This minimum-spanning tree includes 25 OXA-48 producing isolates, 3 non-carbapenemase producing isolates and 3 unknown (isolates from outside UHW).

Epidemiological characteristics:

- Twenty-one patients were inpatients in UHW and two affiliated acute hospitals; St Lukes General Hospital Kilkenny (SLGH) and South Tipperary General Hospital (STGH) (see fig. 2). One isolate was detected from a community sample.
- 15 inpatients were deemed to have hospital-acquired OXA-48 hvKP, while 6 inpatients were deemed to be community-acquired (see table 1).
- In UHW, seven of the HA cases were linked with one CPE outbreak ward over a six-month period, two were linked with two other CPE outbreak wards and one was unknown. This was in the context of ongoing OXA-48 outbreaks on these wards. Eight of the HA cases had previous surveillance swabs with CPE not detected, the remaining two had no previous CPE surveillance swabs.
- In SLGH, four of the inpatients (three CA and one HA) were residents in the same long-term care facility.
- In STGH, the first case identified was a CA case admitted from a long-term care facility. Two of the HA cases were known contacts of confirmed cases. All five patients were linked to the same ward, over a five-week period. All five patients had previous surveillance swabs with CPE not detected, four of which were from the same admission (the four HA cases).
- One patient from each STGH and SLGH had a recent admission to a UHW outbreak ward.

Figure 2. The geographic location of the acute hospitals where hypervirulent OXA-48 *K. pneumoniae* ST23 was isolated from clinical or surveillance specimens during the two-year review period. The numbers within the red circles represent the total number of inpatients from which hypervirulent OXA-48 ST23 *K. pneumoniae* was isolated in that hospital.

	HA	CA
UHW	10	1
SLGH	1	4
STGH	4	1

Table 1. The breakdown of patients with hospital-acquired versus community-acquired OXA-48 hvKp ST23 across the affiliated acute hospitals.

Clinical characteristics:

- Nineteen isolates were detected from faecal surveillance specimens, while six were from clinical specimens; urine cultures n=3, blood cultures n=2, wound swab n=1, PEG site swab n=1.
- One patient colonised with HA OXA-48 hvKP ST23 developed OXA-48 *K. pneumoniae* urosepsis (ST not tested) requiring ICU admission.
- One patient colonised with HA OXA-48 hvKp ST23 was treated for intra-abdominal sepsis requiring ICU admission.
- One patient colonised with HA OXA-48 hvKp ST23 later developed an OXA-48 hvKp ST23 bloodstream infection.
- One patient was admitted with a CA OXA-48 hvKp ST3 bloodstream infection.

Discussion

This study describes the first cluster of carbapenemase-producing hvKp ST23 reported in Ireland. Globally, the majority of hvKp strains belong to a small collection of clonal groups, with CG23, which includes sequence types 23, 26, 57 and 1633, being the most dominant[2]. Of these, ST23 is the most frequently observed hvKp worldwide[2,4] and is the sequence type seen in our region. National data suggests that within Ireland, this cluster of OXA-48 hvKp ST23 is unique to the SE.

This report describes nosocomial transmission and acquisition of hvKp. However, the index cases within the hospital settings are unknown and the possibility of hospital and/or community or environmental reservoirs of hvKp must be considered in future research.

This report also provides further evidence for the convergence of hypervirulence and antibiotic resistant determinants in *K. pneumoniae* strains. Globally, two types of convergence have been described: cKp isolates acquiring virulence genes or plasmids or hvKp isolates acquiring chromosomal or plasmid-encoded antibiotic resistance genes[2]. In this report we describe the latter, a ST23 hvKp strain carrying the OXA-48 gene.

The emergence of carbapenemase-producing hvKp strains represents a significant public health threat and poses additional challenges in the management of infections caused by hvKp. Work is ongoing in our institution, in conjunction with the CPE national reference laboratory, to further characterise the significance and epidemiology of this strain in the region, in addition to establishing a process for hvKp HCAI surveillance.

References

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