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Carbapenem-Resistant *Klebsiella pneumoniae* in Los Angeles:

A Descriptive Analysis of Cases at One Hospital

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Background

- Carbapenem-resistant (CR) *Klebsiella pneumoniae* (KP) were initially discovered in North Carolina in 2001, and have been predominantly described in the Northeastern United States and other select regions of the world.
- The genes encoding carbapenem-resistance are typically plasmid encoded, and are frequently associated with other drug resistance genes. This may facilitate transfer of high-level drug resistance to other *Enterobacteriaceae*, highlighting the significance of this pathogen.
- Despite its clinical significance, there is little data describing the clinical epidemiology of CRKP on the US West Coast.
- We coordinated with our local health department to describe the epidemiology of this emerging highly-drug resistant bacteria in our geographic region

Methods

- Retrospective observational study of inpatients at Cedars-Sinai Medical Center, a 920-bed tertiary care community teaching hospital.
- Hospital laboratory records were reviewed to identify all unique patients with clinical culture positive for CRKP per CLSI criteria between September 2009 and March 2012.
- Carbapenem resistance breakpoints:
  - Before June 2010: Imipenem and Meropenem MIC ≥ 16; Ertapenem MIC ≥ 8
  - June 2010- Present: Imipenem, Meropenem, and Doripenem MIC ≥ 4; Ertapenem MIC ≥ 1
- Clinical infection was identified from chart review of physician documentation.
- Prior history of CRKP was identified in collaboration with LA County Public Health (LAC)
  - CRKP positive patients identified from the study were cross-referenced with a surveillance database to identify prior positives reported to LAC from other health care facilities (HCF).
    - LAC declared CRKP laboratory reportable in June 2010
    - All laboratories identifying a CRKP positive specimen were required to report basic demographic information and submit a full lab report including susceptibility testing
  - LAC contacted the HCF from which our cases were admitted to gather epidemiologic data via survey.

Results

Figure 1. CRKP Cases by Month

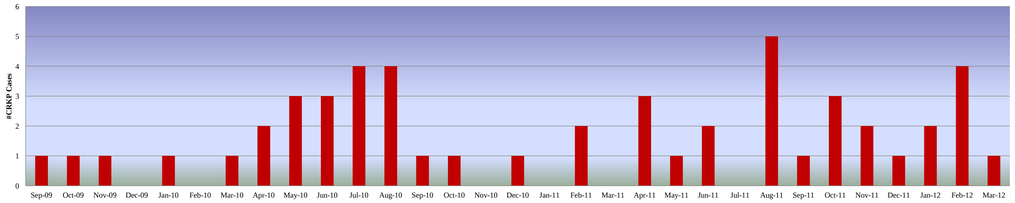


Table 1. Patient Demographics and Risk Factors

Total # of cases	51
Gender distribution	51% Female
Median age	69 years
Median length of stay	14 days
Patients requiring ICU care during hospitalization	25 (49%)
Patients admitted from or discharged to another acute/chronic healthcare facility	35 (69%) (6 from one facility)
Admitted for any infection-related reason	36 (71%)
CRKP Clinical Infection vs. Colonization	40 (78.4%) vs. 11 (21.6%) 27 (53%) of CRKP from urine
Risk Factors	# Patients (%)
Transplant	3 (6%)
Cancer	16 (31%)
Diabetes	20 (39%)
CKD	13 (25%)
Liver disease	7 (14%)
Neurologic disease	24 (47%)
Chronic lung disease	13 (25%)
Patients with prior CSMC inpatient admission within past year	28 (55%)
Devices present within 48 hours of CRKP identification	# Patients (%)
Ventilator/Tracheostomy	17 (33%)
Urethral catheter	23 (45%)
Central line	22 (43%)
Enteral feeding tube	23 (45%)

Table 1. Patient Demographics and Risk Factors (cont.)

Patient prior history of other MDRO (within previous 1 year at CSMC)	# Patients (%)
MRSA	13 (25%)
VRE	31 (61%)
ESBL	11 (22%)
Carbapenem-resistant GNR (non KP)	10 (20%)
Clostridium difficile	10 (20%)
Patients with CRKP identified at other HCF prior to CSMC admission	4 (8%); 3 via LAC surveillance and 1 via LAC survey
Patient history of recent antibiotic exposure (within previous 6 months))	# Patients (%)
Carbapenem	20 (39%)
Anti-pseudomonal B lactam	38 (75%)
1st-3rd generation cephalosporin	22 (43%)
Fluoroquinolone	23 (45%)
Aminoglycoside	15 (29%)
TMP-SMX	9 (18%)
CRKP antibiotic resistance profile	%
Aminoglycosides	47%
Fluoroquinoles	94%
TMP-SMX	51%
Nitrofurantoin	100%
Tigecycline (intermediate or resistant)	63%
Median Colistin MIC	1 µ/mL

•10 (20%) patients had a CR gram-negative bacteria (non-KP) identified from clinical culture within 1 year prior to the first CRKP; 8/10 (80%) were isolated from the same clinical site
•14 (27%) patients had a KP (non-CR) identified from clinical culture within 1 year prior to the first CRKP; 10/14 (71%) were isolated from the same clinical site

Clinical Outcomes

- Crude in-hospital mortality was 18% (9/51)
- In-hospital mortality in the infected cohort was 20% (8/40), while mortality in colonized patients was 9% (1/11, p=0.66)
- No patients with CRKP infection were on effective empiric antibiotics at time of culture

Figure 2. Clinical Distribution of CRKP Patients

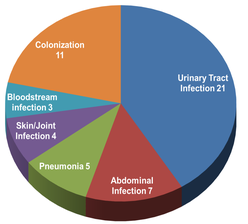


Figure 3. Appropriate Antibiotic Treatment Provided (based on *in vitro* susceptibilities)

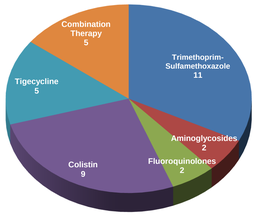
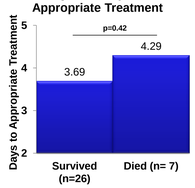


Figure 4. Days to Appropriate Treatment



Discussion

- At a large medical center in Los Angeles, we have demonstrated that patients with CRKP:
  - Are more frequently infected, rather than colonized, with CRKP
  - Always received inadequate empiric therapy due to extensive multi-drug resistance
  - Always have delays in appropriate treatment, with the amount of delay associated with a trend towards higher mortality
  - Are frequent residents of other local healthcare facilities
  - In some cases had CRKP previously identified at another Los Angeles health care facility prior to admission
- For these reasons, increased collaboration between local public health experts and hospital infection control specialists is critical to better communicate risks of CRKP acquisition, and may lead to more effective ways to prevent transmission of and treat CRKP and other MDRO within the community.