

Table 3. Comparison of In-hospital Mortality Among ICU Patients with CRE and CSE

In-Hospital Mortality	Enterobacteriaceae isolate		Total	p-value
	Carbapenem-Susceptible n (%)	Carbapenem-Resistant n (%)		
Survived	95 (74.2%)	79 (61.7%)	174 (68.0%)	0.032
Died	33 (25.8%)	49 (38.3%)	82 (32.0%)	

Disclosures. All authors: No reported disclosures.

496. Carbapenem-resistant *Enterobacter*: A Case-Case-Control Investigation

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Background. *Background.* The World Health Organization has declared carbapenem-resistant *Enterobacteriaceae* (CRE) as a worldwide public health threat. Analyzing the epidemiology of CRE was derived from cohorts consisting primarily of *Klebsiella pneumoniae* isolates. The second most frequent CRE is *Enterobacter* (CREn), but its molecular and clinical epidemiology differ from that of *K. pneumoniae*, and it has not been analyzed while implementing updated methodological tools and design.

Methods. A matched case-case-control investigation was conducted at Shamir (Assaf Harofeh) Medical Center, Israel, for calendar years 2007–2017. Each CREn case was matched to a carbapenem-susceptible *Enterobacter* (CSEn) case and to an uninfected control (1:1:1 ratio). Logistic and Cox regression-matched analyses were conducted in order to study predictors and outcomes of CREn colonization and/or infection, respectively.

Results. The study included 216 cases (72 in each group). Numerous predictors were significantly associated with CREn as per bivariable analyses, but the only independent significant predictors were: (1) recent (3 months) exposure to fluoroquinolones (aOR=2.94, $P = 0.04$), (2) intensive care unit stay in current hospitalization prior to culture (aOR=3.56, $P = 0.003$), and (3) a rapidly fatal McCabe score (aOR=0.471, $P = 0.01$). Patients with CREn suffered from significant delays in instituting appropriate antimicrobials ($P = 0.03$), and for those who survived the hospitalization, were more frequently discharged to a long-term care facility after being admitted to the index hospitalization from home (aOR=3.3, $P = 0.02$).

Conclusion. This case-case-control-matched investigation of CREn epidemiology, revealed a unique modifiable predictor, i.e., recent fluoroquinolone exposure, which could represent a target for stewardship intervention. The case-case-control-matched design allowed for the control of numerous confounders previously reported to be associated with CREn but may represent a risk factor for *Enterobacter* infection in general. As with other CRE, CREn carriers suffer from significant delays in institution of appropriate antimicrobials and from worse outcomes.

Disclosures. All authors: No reported disclosures.

497. Changing Molecular Epidemiology of CRE from 2016–2018, Increase in the Unknown

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Background. Historically, endemic *Klebsiella pneumoniae* carbapenemase (KPC) has accounted for the majority of carbapenem-resistant *Enterobacteriaceae* (CRE) in Los Angeles County (LAC). The LAC Department of Public Health (DPH) initiated enhanced CRE surveillance in 2016 to determine CRE prevalence and track emerging non-KPC resistance mechanisms (IMP, NDM, OXA, and VIM) among CRE to describe characteristics and identify local epidemiology for novel multi-drug-resistant organism (N-MDRO) infection and colonization.

Methods. CRE isolates were voluntarily submitted by local clinical laboratories for mechanism detection by LAC Public Health Laboratory via MALDI-TOF and Nanosphere BC-GN. Baseline isolates were collected in 2016. Results are then presented by year through 2018. For N-MDRO cases, LACDPH interviewed healthcare facility (HCF) staff and cases to obtain case characteristics. Data were analyzed via Microsoft Access and SAS.

Results. CRE surveillance isolates were voluntarily submitted by 31 labs representing 34% (34/96) LAC hospitals and 1 large regional lab serving 60% of skilled nursing facilities from January 2016 to December 2018. LACDPH tested 1438 CRE isolates during the study period, 1168 (81%) were carbapenemase producing (CP). The proportion of CP CRE and KPC CRE declined over the study period (Table 1). NDM

was the most common non-KPC ($n = 30$) followed by OXA ($n = 28$). The proportion of CRE with no genotypic marker increased over the course of the study. Case characteristics were obtained from 41 non-KPC CP CRE cases; median age was 66 years (range: 6–94 years); 12 (29%) expired. Among the 41 cases, 20 (49%) had a central line; 11 (27%) had surgery; 14 (34%) had antibiotics in the 6 months prior to culture date. Of the 41 cases, 11 (27%) had international healthcare exposure within 12 months with an invasive procedure and/or antibiotics.

Conclusion. Surveillance in a large urban setting suggests the molecular epidemiology of CRE is changing, with declining prevalence of KPC, increasing metallo-β-lactamase CP, and large proportion of isolates without resistance markers detected. Given the worrisome trends in non-KPC CRE, more systematic surveillance is warranted, potentially using more robust molecular epidemiology.

Table 1. Enhanced CRE Surveillance 2016–2018 (n=1438).

Year	Total Isolates	CP-CRE (%)	CP-CRE/Total Isolates (%)	KPC (%)	KPC (%)	VIM (%)	VIM (%)	OXA (%)	OXA (%)	NDM (%)	NDM (%)	IMP (%)	IMP (%)	No marker detected	No marker/Total Isolates (%)
2016	520	432	83%	422	81%	1	0.2%	5	1%	4	1%	0	0%	88	17%
2017	487	422	87%	400	82%	0	0%	14	3%	6	1%	2	0.4%	65	13%
2018	431	314	73%	283	66%	2	0.5%	9	2%	20	5%	0	0%	117	27%
Total	1438	1168	81%	1105	77%	3	0.2%	28	1.9%	30	2.1%	2	0.1%	270	18.8%

Disclosures. All authors: No reported disclosures.

498. High Burden of CRO Colonization and Its Association with Infection Among Patients transferred to a Tertiary Care Hospital in India

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Background. Infections with carbapenem-resistant organisms (CRO) are increasing worldwide and are associated with high mortality. Patients transferred from outside hospitals have been reported to be at increased risk of CRO colonization and infection. The rate of subsequent CRO infection in patients colonized with CRO is unclear in a high CRO burden setting

Methods. Medanta Hospital in Gurgaon, India instituted CRO colonization screening for patients transferred from outside hospitals for infection control purposes. From April 2018 to May 2018, patients transferred from other hospitals to the intensive care unit at Medanta were subjected to CRO colonization screening using Xpert Carba R (Cepheid) performed on the day of transfer. Subsequent recovery of CRO in cultures of blood, bronchoalveolar lavage fluid, urine in specimens with pyuria obtained from patients without urinary catheters, pus, and tissue were considered to be indicative of CRO infection. The association of CRO colonization with subsequent CRO infection was assessed with a Fisher exact test

Results. Among 457 patients screened, 205 patients (45%) were found to be colonized with CRO at admission. Genes for New Delhi Metallo-β-lactamase (NDM) were detected in 184 (40%) patients, OXA-48 in 97 (21%) patients, VIM in 18 (4%) patients, KPC in 5 (1%) patients, and IMP1 in 5 (1%) patients; >1 carbapenemase gene was detected in 95 (21%) patients. CRO infections were observed in 25 (5%) patients including 12 with bacteremia, 7 with pneumonia, 4 with urinary tract infection, and 2 with soft-tissue infection. Among patients with CRO colonization, 17 (8%) patients developed CRO infection during the course of hospitalization; among patients without admission CRO colonization, subsequent CRO infection was found in 8 (3%) patients. CRO admission colonization was associated with subsequent clinical infection with CRO (odds ratio = 2.8, $P = 0.02$)

Conclusion. CRO colonization was found in almost half of patients transferred from outside hospitals to a large tertiary care hospital in India and was associated with subsequent CRO infection. Further work is necessary to understand the role of CRO colonization screening in infection control and antimicrobial stewardship in a setting with high CRO burden

Disclosures. All authors: No reported disclosures.

499. Carbapenem-resistant *Enterobacteriaceae* (CRE)-associated Infections and Prolonged Colonization among Hospitalized Patients Colonized by CRE

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Background. This study aims to determine rates of subsequent carbapenem-resistant *Enterobacteriaceae* (CRE)-associated infections and prolonged colonization among patients colonized by CRE and to identify risk factors of such conditions.

Methods. This study was conducted among a cohort of hospitalized adult patients colonized by CRE at any sites from June 1, 2015 to December 31, 2018. The patients had been prospectively identified by the Infection Control (IC) Division of a Thai tertiary-care hospital. According to the hospital's IC protocol, patients with CRE colonization/infections were isolated and underwent CRE cultured at the colonized/infected sites every week until the cultures have turned negative for 2 consecutive times. Prolonged colonization was defined as having CRE colonization more than 30 days.

Results. Of the 125 patients identified, 25 were excluded due to death, being transferred, or discharged within 48 hours of CRE colonization detected. The final

cohort included 100 patients, the median age was 74 years, 48% were male, the most common colonized site was rectum (37%) and 20 patients (20%) developed subsequent CRE-associated infections. The median time from colonization to infection was 13 days and the most common site of infection was bloodstream (45%). Independent factors associated with subsequent CRE-associated infections were the number of colonization sites [adjusted odds ratio (aOR) 7.98, $P < 0.001$], central line insertion during admission (aOR 7.97, $P = 0.009$) and receipt of vancomycin during admission (aOR 24.77, $P = 0.02$). Prolonged colonization was observed in 13 of 77 evaluable patients (17%). There were trends toward significance that the length of hospital stay and duration of antibiotic prior to colonization were associated with prolonged colonization ($P < 0.10$).

Conclusion. The findings suggest high rates of subsequent CRE-associated infections and prolonged colonization among the study population. Patients with risk factors for subsequent infections should be closely monitored and empirically-treated with antibiotics active against CRE while those with risk factors for prolonged colonization should receive continued surveillance and isolation to prevent CRE transmission.

Disclosures. All authors: No reported disclosures.

500. Prevalence of Extended-Spectrum β -lactamase and Carbapenem-Resistant Gram-Negative Bacteria in Patients with Urinary Tract Infection and Urosepsis Admitted through Emergency Departments in the United States

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Background. Gram-negative infections due to extended-spectrum β -lactamase (ESBL)-producing Enterobacteriaceae, and carbapenem-resistant Enterobacteriaceae (CRE) and non-fermenting (CR-NF) strains, are increasingly encountered. Study objectives were to determine prevalence and associated risk factors and outcomes for these strains among emergency department patients hospitalized for urinary tract infection (UTI) at 11 US hospitals.

Methods. This was a prospective observational study of patients ≥ 18 years hospitalized for UTI. Clinical data were collected at the index visit. Urine was obtained for culture and susceptibility testing. Electronic medical record and telephone follow-up were conducted after 30 days for site laboratory results, treatment, and clinical outcomes. Positive culture was defined as 1 uropathogen with growth at $\geq 10^4$ cfu/mL, or 2 with 1 or both at $\geq 10^5$ cfu/mL, or ≥ 3 with 1 or 2 at $\geq 10^5$ cfu/mL. Isolates with ceftriaxone (CRO) or meropenem MIC > 1 $\mu\text{g/mL}$ will undergo reference laboratory (IHMA, Inc., Schaumburg, IL) susceptibility testing, including against newer antibiotics and cefiderocol.

Results. We enrolled 774 participants between 2018 and 2019; 289 (37.3%) excluded due to urine culture not done, no growth, or contamination. Of 485 culture-positive participants (median age 56 years, 62.0% female), 432 (89.1%) grew 1 uropathogen, 48 (9.9%) 2, and 5 (1.0%) ≥ 3 . Prevalences of CRO-resistant Enterobacteriaceae, CRE, and CR-NF were 19.9%, 2.1%, and 10.7%, respectively. At sites, 95.7% of CRO-resistant Enterobacteriaceae isolates were ESBL. Among participants with any or no antibiotic resistance risk factors, i.e., antibiotics, hospitalization, long-term care, or travel within 90 days, prevalence of CRO-resistant Enterobacteriaceae was 68/228 (29.8%) and 10/155 (6.5%), respectively. Among those with CRO-resistant vs. susceptible Enterobacteriaceae infections, ICU admission and death occurred in 9.9% vs. 6.6% and 3.7% vs. 1.0%, with median time home over 30 days, 24 vs. 27 days, respectively.

Conclusion. Among US hospitalized patients with UTI, infections due to CRE remain uncommon; however, ESBL and CR-NF now account for a substantial proportion of cases and are associated with resistance risk factors and worse outcomes.

Disclosures. All authors: No reported disclosures.

501. Risk of Infection in Persons Colonized with Carbapenemase-Producing Enterobacteriales (CPE) in Ontario, Canada

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Background. We aimed to assess the risk of subsequent infection among patients colonized by CPE.

Methods. The Toronto Invasive Bacterial Diseases Network (TIBDN) has conducted population-based surveillance for CPE colonization/infection in Toronto and Peel region, Ontario, Canada, since CPE were first identified (2007). All laboratories report all CPE isolates to TIBDN. Clinical data are collected via patient interview and hospital chart review. Initially colonized patients are followed for 5y; subsequent CPE infection is defined as an episode with onset > 3 days after initial detection of CPE colonization that meets National Healthcare Safety Network criteria for infection with a clinical isolate of CPE.

Results. From 2007 to 2018, 790 persons with CPE colonization/infection were identified. Among 364 cases colonized at identification, 42 (12%) subsequently had at least one clinical isolate, and 23 (6%) had an infection: 8 with bacteremia (primary or secondary), 7 UTI, 5 pneumonia, and 3 other. The median time from identification of colonization to infection was 21 days (IQR 7–38), with a probability of developing an infection of 7% at 3 months, and 18% by 3 years (figure). In 305 cases with data available to date, older persons, those admitted to the ICU, and those with current/recent invasive medical devices were more likely to develop infection (table). Gender, underlying conditions and other procedures were not associated with risk of infection. There was a trend to infections being more likely in patients colonized with *K. pneumoniae* (52% vs. 35%, $P = 0.13$).

Conclusion. The risk of subsequent infection in our cohort was 18%, with highest risk in the first 3 months; most infections occurred in patients requiring intensive care unit admission and invasive medical devices.

Figure. Cumulative probability of subsequent CPE infection among patients colonized with CPE.

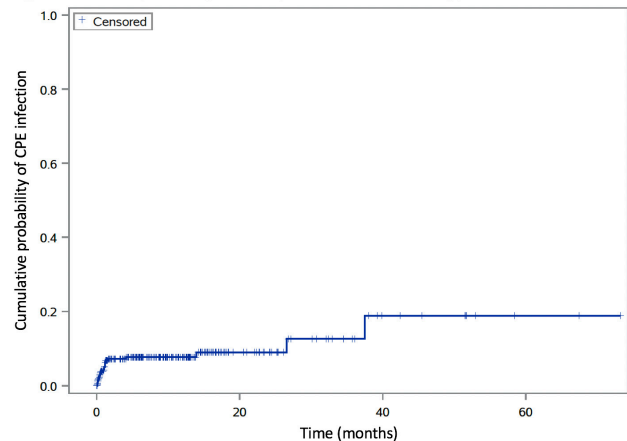


Table. Selected characteristics in patients who did and did not develop infection.

Characteristics	Developed infection n = 18	Colonized only n = 287	P
Age, years (median, IQR)	63 (46-72)	69 (55-78)	.03
Transferred from another hospital	7 (39%)	42 (15%)	.007
Invasive devices (current or within last year)			
Central venous line	11 (61%)	60 (21%)	<.001
Chest tube	4 (22%)	9 (3%)	<.001
Urinary catheter	14 (78%)	100 (35%)	<.001
Admitted to ICU	15 (83%)	78 (27%)	<.001
Requiring mechanical ventilation	11 (61%)	38 (13%)	<.001
Receiving hemodialysis	5 (28%)	27 (9%)	.01

Disclosures. All authors: No reported disclosures.

502. Klebsiella variicola Infections in Service Members Who Sustained Trauma in Iraq and Afghanistan

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Background. Recent work has argued that genus *Klebsiella* is best divided into 3 clades: *K. pneumoniae* (Kp), *K. quasipneumoniae* (Kq), and *K. variicola* (Kv). Kv has drawn attention from reports of higher mortality and virulence. We evaluated a previously defined group of military trauma patients with *Klebsiella* infections for the presence of Kv, described clinical and isolate characteristics, and compared Kv and Kp groups.

Methods. All initial and serial (≥ 7 days from prior isolate) infecting Kp isolates (identified by clinical laboratories without the ability to speciate Kq and Kv)