492. High Prevalence of Colonization with Carbapenem-Resistant Enterobacteriaceae Among Patients Admitted to Vietnamese Hospitals: Risk Factors and Burden of Disease

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Background. Carbapenem-resistant Enterobacteriaceae (CRE) is an increasing problem worldwide, but particularly problematic in low- and middle-income countries (LMIC) due to limitations of resources for surveillance of CRE and infection prevention and control (IPC).

Methods. A point prevalence survey (PPS) with screening for colonization with CRE was conducted on 2233 patients admitted to neonatal, pediatric and adult care at 12 Vietnamese hospitals located in northern, central and southern Vietnam during 2017 and 2018. CRE colonization was determined by culturing of fecal specimens on selective agar for CRE. Risk factors for CRE colonisation were evaluated. A CRE admission and discharge screening sub-study was conducted among one of the most vulnerable patient groups; infants treated at an 80-bed Neonatal ICU from March throughout June 2017 to assess CRE acquisition, hospital-acquired infection (HAI) and treatment outcomes.

Results. A total of 1165 (52%) patients were colonized with CRE, most commonly Klebsiella pneumoniae (n = 805), Escherichia coli (n = 682) and Enterobacter spp. (n = 61). Duration of hospital stay, HAI, intubation, peripheral venous catheter and treatment with a carbapenem were independent risk factors for CRE colonization. The PPS showed that the prevalence of CRE colonization increased on average 4.2% per day and mean CRE colonization rates increased from 13% on the day of admission to 89% at day 15 of hospital stay. At the NICU CRE colonization increased from 32% at admission to 87% at discharge, mortality was significantly associated (OR 5.5, P < 0.01) with CRE colonisation and HAI on admission.

Conclusion. These data indicate that there is an epidemic spread of CRE in Vietnamese hospitals with rapid transmission to hospitalized patients. CRE colonization places a major burden on the healthcare system due to the increased risk of HAI caused by CRE and associated increased mortality. This study shows that large-scale epidemiological surveillance of CRE using affordable methods is possible in low- and middle-income countries.

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493. Laboratory Evaluation and Epidemiology of Carbapenemase-Producing Carbapenem-Resistant Enterobacteriaceae in Department of Veterans Affairs, 2017

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Background. Carbapenemase-producing (CP)-carbapenem-resistant Enterobacteriaceae (CRE) pose a major threat to public health and are a priority for national prevention and control efforts including within Department of Veterans Affairs (VA). The laboratory evaluation and epidemiology of CRE in VA is uncertain.

Methods. Using data from the Veterans Health Administration Corporate Data Warehouse, we identified all Veterans with ≥1 CRE result obtained during 2017 and reviewed their electronic health record. Two case definitions were used: (1) 2015 CDC CRE (Enterobacteriaceae resistant to any carbapenem or with documented carbapenemase production) and (2) 2017 VA CP-CRE (E. coli, Klebsiella spp., and Enterobacter spp. resistant to imipenem, meropenem, or doripenem or with documented carbapenemase production). Patients harboring carbapenemase-producers detected by rectal screening tests only were included. We reviewed patient charts whose isolates met both CRE definitions, extracting detailed microbiologic and travel data for the first positive 2017 result.

Results. We identified 904 unique Veterans with CRE, 577 (64%) patients had results meeting both CRE case definitions while 327 (36%) had results meeting CDC CRE criteria only (Figure 1). Of the 458 patients with clinical isolates meeting both case definitions, urine specimens predominated (64%) and were associated with the lowest crude 90-day mortality (16%); mortality was highest amongst patients with respiratory tract cultures (40%) and bloodstream isolates (34%) (Figure 2). Nearly half (48%) of VA CP-CRE were tested for carbapenemases (76% in-house; 24% send-out); of these, 75% tested positive with 78% being a KPC, 1% NDM, and 21% unspecified (Figure 3). Additionally, all 119 CRE carriers with an identified gene had KPC. Only 7 patients (1%) had documented overseas travel.

Conclusion. Currently the incidence of CP-CRE in the nation’s largest healthcare system is low relative to other problem pathogens such as MRSA and Clostridium difficile but is associated with a high crude mortality especially with respiratory and bloodstream isolates. KPC comprised almost all carbapenemases identified. This provides an initial, granular snapshot of CRE in VA to serve as a roadmap for ongoing CP-CRE prevention and control.

Figure 1: Incidence of CRE in VA, 2017

| Result Type* | Incidence (2017 patient years n = 1,823,140) |
|-------------|-----------------------------------------------|
| VA CP-CRE   | 458  51%                                        |
| CRE Screen only | 119  13%                                        |
| CDC CRE only | 327  36%                                        |
| Total CRE   | 904  100%                                      |

*Result Type Definitions
VA CP-CRE: All clinical cultures meeting 2017 VA CP-CRE also meet the 2015 CDC CRE definition.
CRE Screen only: Rectal or perirectal swab-positive cases without clinical cultures — i.e., patients identified achieving CP-CRE colonization; this meets both CRE case definitions.
CDC CRE only: CDC CRE only consist of clinical cultures meeting the 2015 CDC CRE definition but not the 2017 VA Suspected CP-CRE definition.

**Incidence calculated using “2017 patient years” as denominator, which represents the number of Veterans who accessed the VA system for medical care nationally in 2017.

Figure 2: VA CP-CRE Specimen Type and Associated Crude 90-day Mortality

| Specimen Type | n | 90-Day Mortality (n) |
|---------------|---|---------------------|
| Urine         | 293 | 16% |
| Respiratory Tract | 55 | 22% |
| Wound         | 46  | 23% |
| Blood         | 29  | 10% |
| Total         | 458 | 22% |
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494. Fitness Cost of mcr-1-Mediated Colistin Resistance in Carbapenemase-Producing Klebsiella pneumoniae
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Background. The emergence of mobile colistin resistance gene mcr-1, a plasmid-borne polymyxin resistance mechanism, in carbapenem-resistant Klebsiella pneumoniae is an alarming concern. However, previous studies showed that the acquisition of mcr-1 was associated with a significant biological fitness cost in K. pneumoniae. We aimed to study the impact of mcr-1 on the biological fitness in clinical carbapenemase-producing K. pneumoniae strains.

Methods. Clinical carbapenemase-producing K. pneumoniae strains were collected consecutively at the Taipei Veterans General Hospital between November 2017 and December 2018. The strain positive for mcr-1 was subjected to whole-genome sequencing to delineate its genomic features. Escherichia coli J53 strain was used as the recipient strain in plasmid conjugation assay and the transconjugants were selected with sodium azide and colistin. Plasmid stability was tested by serial passage in antibiotic-free LB broth for 28 days. The growth rate was compared between the parental mcr-1-bearing strain and the plasmid-cured strain.

Results. One ST11 strain isolated from a fatal case with bacteremia (KP2509) was found to harbor blaKPC-2, blaoxa-48 and mcr-1. This strain was resistant to colistin (MIC=8 mg/L) and imipenem (MIC=216 mg/L). Whole genome sequencing of KP2509 showed that mcr-1, blaKPC-2, and blaoxa-48 were located on an IncHI-FIB type plasmid of 319 Kb, an IncFI type plasmid of 96 Kb, and an IncL type plasmid of 64 Kb, respectively. Conjugation efficiency of mcr-1-bearing plasmid was 2.24 x 10^-7, and the mcr-1-bearing plasmid in KP2509 showed high plasmid stability, and only ~1% were lost after 27-day passages. The resulting plasmid-cured strain (PC-KP2509) was susceptible to colistin (MIC=0.5 mg/L) and had a similar growth rate to that of parental mcr-1-bearing strain KP2509.

Conclusion. We identified an ST11 K. pneumoniae strain carrying mcr-1 and mcr-1 genes causing a fatal bacteremia. The large mcr-1-bearing plasmid confers a moderate level of colistin resistance but without significant biological fitness cost in carbapenemase-producing K. pneumoniae, which could result in a serious threat clinically.

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495. Risk Factors of Carbapenem-Resistant Enterobacteriaceae (CRE) Infections Among Intensive Care Unit (ICU) Patients in a Tertiary Hospital in the Philippines
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Background. The threat of Carbapenem-Resistant Enterobacteriaceae (CRE) is increasing worldwide, and the epidemiology, risk factors, and outcomes of CRE in the Philippines is unknown.

Methods. We performed a retrospective case–control study of 128 CRE cases and Carbapenem-Susceptible Enterobacteriaceae (CSE) controls matched 1:1 based on site of infection and date of admission among all adult patients in the Intensive Care Unit (ICU) between January 2014 and May 2018 at The Medical City. Predictors of CRE infection among matched cases and controls were determined through multiple conditional logistic regression analysis. In-hospital mortality was analyzed using z-test of two proportions and length of stay among patients with CRE and CSE were compared.

Results. The mean age in both groups was similar at 65.8 (range 23–92) and 64.9 (range 23–98) years, respectively. There were more males among cases than controls [(76/128, 59%) vs. 62/128 (48%)]. Those with CRE were more likely to have a co-morbid illness and an invasive device. Pneumonia was the most common site of CRE infection (40%) followed by the urinary tract (27%). Enterobacter cloacae (54.68%) was the most common organism, followed by Klebsiella pneumoniae (30.46%). On univariate analysis, the use of piperacillin–tazobactam, third or fourth-generation cephalosporins and carbapenems, mechanical ventilation, and acute kidney injury (AKI) increased the risk of developing CRE infections by an OR of 7.5 (CI 1.88–29.95, P = 0.004), 9.32 (CI 1.48–58.59, P = 0.017), and 10.76 (CI 1.69–68.53, P = 0.012), respectively. Those with CRE had a higher in-hospital mortality than the CSE group [(49/79, 38.3%) vs. (33/95, 25.8%); P = 0.032]. Length of hospital stay among CRE cases was also longer with a mean of 43.9 vs. 28 days, 28 days compared with controls.

Conclusion. In our cohort, older patients with/without comorbidities developed CRE with pneumonia being the most common site of infection. Prior use of broad-spectrum antimicrobials, mechanical ventilation and AKI appeared to increase the risk of CRE infection in the ICU CRE infection also increased patient mortality and length of hospital stay; Interventions that target these risk factors should be undertaken to help prevent CRE infection.

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