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 colonisation 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 outcome.

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 colonisation rates increased from 13% on the day of admission to 89% at day 15 of hospital stay. At the NICU CRE colonisation 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 target of 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 *Clostridioides 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*	n	%	Incidence** (2017 patient years n = 1,823,140)
VA CP-CRE	458	51%	0.0251%
CRE Screen only	119	13%	0.0065%
Results meeting both case definitions	*577*	*64%*	*0.0316%*
CDC CRE only	327	36%	0.0179%
Total CRE	**904**	**100%**	**0.0496%**

*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 as having 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)	90-Day Mortality (%)
Urine	293	64%	47	16%
Respiratory Tract	55	12%	22	40%
Wound	46	10%	13	28%
Other	35	8%	8	23%
Blood	29	6%	10	34%
Total	**458**	**100%**	**100**	**22%**

Figure 3: CRE Species Distribution and Carbapenemase Testing Results

Species	VA Suspected CP-CRE Identified n	%	Tested for Carbapenemase n	%	Positive Carbapenemase Tests n	%	Genotypic Data from Positive Carbapenemase Tests Gene Identified	n
Klebsiella pneumoniae	245	53%	139	57%	128	92%	KPC	109
							Not specified	19
Enterobacter cloacae	103	22%	47	46%	18	38%*	KPC	8
							NDM	1
							Not specified	9
Escherichia coli	61	13%	12	20%*	6	50%*	KPC	5
							Not specified	1
Klebsiella aerogenes (formerly E. aerogenes)	29	6%	13	45%	4	31%*	KPC	1
							Not specified	3
Klebsiella oxytoca	15	3%	6	40%	5	83%	KPC	3
							Not specified	2
Enterobacter spp. other	11	2%	7	64%	6	86%	KPC	5
							Not specified	1
Total	**463**	**100%**	**224**	**48%**	**167**	**75%**	**KPC**	**131** **78%**
							NDM	**1** **1%**
							Not Specified	**35** **21%**

Five cultures had more than one organism identified. *Significantly different from *K. pneumoniae* as the reference organism at the p=0.05 level.

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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 passaging 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 bla_{KPC-2}, bla_{OXA-48}, and *mcr-1*. This strain was resistant to colistin (MIC=8 mg/L) and imipenem (MIC≥16 mg/L). Whole-genome sequencing of KP2509 showed that *mcr-1*, bla_{KPC-2} and bla_{OXA-48} were located on an IncHI-FIB type plasmid of 319 Kb, an IncFII type plasmid of 96 Kb, and an IncL type plasmid of 64 Kb, respectively. Conjugation efficiency of *mcr-1*-bearing plasmid was 2.24×10^{-4}, and the colistin MIC of *E. coli* J53 transconjugant increased from 0.5 to 8 mg/L. 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 bla_{KPC-2}, bla_{OXA-48}, 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 64.3 (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 compared with controls.

Conclusion. In our cohort, older patients w/ 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.

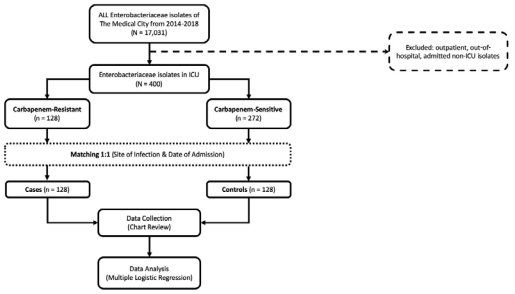

Table 1. Demographic and Clinical Characteristics of Patients

Demographic and Clinical Characteristics	CRE group n=128	CSE group n=128	p-value
Age [a]	65.8 (15.0)	64.3 (19.9)	0.4184
Sex			
Male	76 (59%)	62 (48%)	0.0729
Female	52 (41%)	66 (52%)	
Hypertension	82 (64%)	66 (52%)	< 0.04
Heart failure	98 (77%)	7 (5%)	< 0.0001
Diabetes	64 (50%)	41 (32%)	< 0.0051
Malignancies	25 (20%)	18 (14%)	0.24
Use of Antibiotics			
Piperacillin-tazobactam	98 (77%)	17 (13%)	< 0.0001
3rd or 4th generation cephalosporin	86 (67%)	10 (8%)	< 0.0001
Fluoroquinolones	56 (44%)	11 (9%)	< 0.0001
Carbapenem	65 (51%)	5 (4%)	< 0.0001
Vancomycin	21 (16%)	4 (3%)	0.0003
Ventilator Use			
Used ventilator	100 (78%)	63 (49%)	< 0.00001
Did not use ventilator	28 (22%)	65 (51%)	
Central Vascular Access			
With central vascular access	85 (66%)	40 (31%)	< 0.00001
Without central vascular access	43 (34%)	88 (69%)	
Acute Kidney Injury (AKI)			
With AKI	46 (36%)	21 (16%)	< 0.0006
Without AKI	82 (64%)	107 (84%)	
Percutaneous Catheterization			
Used catheter	47 (37%)	57 (45%)	0.2528
Did not use catheter	81 (63%)	71 (55%)	

a - mean (standard deviation / SD)

Table 2. Results of Multiple Conditional Logistic Regression

Predictors	Adjusted OR (95% CI)	p-value
Age	0.95 (0.87 – 1.03)	0.199
Central Vascular Access	0.19 (0.10 – 3.60)	0.268
Heart Failure	0.44 (0.03 – 7.60)	0.573
Hypertension	0.12 (0.05 – 3.12)	0.205
Diabetes	46.92 (0.71 – 88.41)	0.098
Ventilator Use	9.32 (1.48 – 58.59)	0.017
Acute Kidney Injury	10.76 (1.69 – 68.53)	0.012
Use of Piperacillin-tazobactam	7.50 (1.88 – 29.95)	0.004
Use of 3rd or 4th generation cephalosporin	17.16 (2.41 – 122.32)	0.005
Use of Fluoroquinolones	2.61 (0.24 – 28.30)	0.429
Use of carbapenem	13.91 (1.82 – 106.58)	0.011
Use of Vancomycin	4.11 (0.04 – 393.19)	0.544