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Risk factors for colonization of carbapenemase-producing Enterobacteriaceae in the intensive care unit

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INTRODUCTION

- Carbapenem-resistant Enterobacteriaceae (CRE), particularly carbapenemase producing Enterobacteriaceae (CPE), is an emerging threat worldwide.
- In Asia, resistance rates to imipenem and meropenem in *Enterobacteriaceae* exhibited also stably escalating trend during the past decade.
- CPE are a subset of all CRE and produce carbapenemase that break down carbapenems and related antimicrobials making them ineffective.
- CPE have the ability to spread rapidly and can cause infections that are associated with high mortality rates.
- Especially, in intensive care unit (ICU), CPE can result in more dreadful outcome.
- Despite clinical significance of carbapenem resistance in infections caused by *Enterobacteriaceae*, there are few reports regarding the risk factors for colonization of CPE in Korea.
- Therefore, this study was performed to identify risk factors for the colonization of CPE in ICU.

MATERIALS AND METHODS

- Retrospective case-control study (1:4 matched)
- Duration : January 2014 through December 2014
- Medical (16 beds) and surgical (21 beds) at Hallym University Sacred Heart Hospital, university-affiliated, tertiary-care university hospital with 829 beds
- Active surveillance culture for patients admitted to the medical and surgical ICU for >48 hours was performed at ICU admission and once per week and ICU discharge (or within the second day after ICU discharge)
- Case patients were subjects who colonized with CPE in ICU. Control patients were subjects with no evidence of CPE or CRE colonization.
- The controls were matched according to patient sex, age and the admission date.
- We reviewed the medical records of the patients, and the following informatio n was collected from patients chart: age, sex, underlying diseases, comorbid conditions, duration of ICU stay, history of previous admission, presence of indwelling catheter and history of antibiotics treatment
- Immunosuppressant uses include chemotherapeutic agent, immunosuppressant for preventing rejection of transplanted organ and steroid in prior month.
- Species identification and antimicrobial susceptibility testing were performed using the MicroScan Walkaway-96 system and MicroScan Neg BP Combo 42 Panel (Siemens, West Sacramento, CA)
- Carbapenemase production was screened by the modified Hodge test and carbapenemase inhibition test. Carbapenemase types were confirmed by the National Research Institute of Health
- The Student's *t*-test was used to compare continuous variables, and χ^2 or Fisher's exact tests to compare categorical variables. In identifying the independent risk factors for the colonization of CPE, logistic regression model was used to control for the effects of confounding variables. All *P* values were two-tailed, with $P < 0.05$ considered statistically significant.

RESULTS

- 33 patients colonized with CPE *were* identified
- The most common species among CPE was OXA-232 type *Klebsiella pneumoniae* (n=23).
- On univariate analysis, solid cancer (P=0.016), cardiovascular diseases (P=0.037), pulmonary diseases (P=0.013), neurologic diseases (P=0.049), length of ICU stay (P<0.001), mechanical ventilation (P<0.001), previous use of piperacillin/tazobactam (P=0.010), previous use of carbapenem (P=0.005), previous use of colistin (P=0.025), as well as previous use of glycopeptide (P=0.014), were significantly associated with CPE colonization.(**Table**)

Table. Clinical characteristics and risk factors for CPE acquisition

Variables	CPE (n=33)	Control (n=132)	P
Age (median)	69 (IQR 18)	68 (IQR 22)	0.288
Male	20 (60.6%)	80 (60.6%)	0.937
Underlying disease			
Solid tumor	10 (30.3)	17 (12.9)	**0.016**
Hemato. Malignancy	0 (0.0)	1 (0.8)	1.000
Liver disease	2 (6.1)	17(12.9)	0.370
Cardiovascular disease	14 (42.4)	32 (24.2)	**0.037**
Pulmonary disease	19(57.6)	45(34.1)	**0.013**
Neurologic disease	9 (27.3)	61 (46.2)	**0.049**
Renal disease	4(12.1)	18 (13.6)	1.000
Diabetes Mellitus	9(27.3)	35 (26.7)	0.949
Charlson Comorbidity Index	4(IQR 5)	3(IQR 4)	**0.036**
McCabe classification			0.137
Previous admission	16(48.5)	42(31.8)	0.073
ICU duration (mean ±SD)	24.54 (±30))	11.08 (±11.4)	**<0.001**
Comorbid condition			
Central venous catheterization	21(63.6)	74(56.1)	0.431
Ventilator	25(75.8)	52(39.4)	**<0.001**
CRRT	4(12.1)	15(11.4)	0.903
immunosuppressant	2 (6.1)	9 (6.8)	1.000
Foley catheter	30 (90.9)	117(88.6)	1.000
L-tube insertion	28 (84.8)	77(58.3)	**0.005**
Percutaneous tube	10 (30.3)	43 (32.6)	0.803
Invasive procedure	15 (45.5)	55 (41.7)	0.694
Receipt antibiotics	32(97.0)	107(81.1)	**0.030**
Cephalosporins	12 (36.4)	59 (44.7)	0.387
Quinolones	15 (45.5)	57 (43.2)	0.814
Pip/tzb	23(69.7)	59(44.7)	**0.010**
Metronidazole	10 (30.3)	20(15.2)	**0.044**
Carbapenems	19(57.6)	41(31.1)	**0.005**
Colistin	6(18.2)	8(6.1)	**0.025**
Glycopeptides	20(60.6)	49(37.1)	**0.014**

CPE: carbapenemase producing Enterobacteriacea e, CRRT: continuous renal replacement therapy Data are number (%), otherwise indicated.

- On multivariate analysis, length of ICU stay was independently associated CPE colonization (OR, 1.040;95%CI, 1.004-1.076; P=0.029).

CONCLUSIONS

- This study suggests that antimicrobial exposure and length of ICU stay play important roles in the colonization of CPE.