Kohei UECHI1, Tatsuya TADA2, Kayo SHIMADA2, Isamu NAKASONE3, Teruo KIRIKAE2, and Jiro FUJITA3; Division of Clinical Laboratory and Blood Transfusion1, Control and Prevention of Infectious Disease office3, University Hospital of the Ryukyus, Okinawa 903-0125, Japan, Department of Infectious Diseases Research Institute, National Center for Global Health and Medicine, Tokyo 162-8655, Japan2 (June 16–20, 2016): MEPM and CL Heteroresistance in Enterobacteriaceae Isolates in Japan. ASM Microbe 2016 (Boston, MA, USA)
Background: The rapid spread of carbapenem-resistant Enterobacteriaceae (CRE), with the emergence of colistin (CL)-resistant CRE, has become an urgent health concern worldwide. We described here that the first identification of two isolates, a MEPM-heteroresistant Klebsiella pneumoniae and a meropenem (MEPM)-resistant and CL-heteroresistant Enterobacter cloacae.

Methods: We conducted active surveillance to find patients colonized with CRE in a university of Ryukyu hospital in Okinawa Japan. Rectal swabs were screened for CRE using ESBLs selective agar (in house), and CHROMagar KPC (CHROMagar: France) according to Laboratory Protocol for Detection of Carbapenem-Resistant or Carbapenemase-Producing, Enterobacteriaceae. As for the phenotype check, Modified Hodge Test (MHT) and CarbaNP test were performed. Drug susceptibility tests were done by both a two-fold dilution method and disk method/Etest according to CLSI guidelines. Antibiotics heteroresistance was defined as a phenomenon where subpopulations of presumed isogenic bacteria exhibited a range of susceptibility to MEPM or CL. The whole genomes of CRE isolates were determined by sequencing with Illumina’s MiSeq.

Results: Of 20 Enterobacteriaceae isolates, 8 showed MICs of MEPM (2-32 ug/ml). However, MHT and CarbaNP test were negative. of them, a K. pneumoniae isolate showed heteroresistance to MEPM, and an E. cloacae isolate did heteroresistance to CL as determined by using a disk method, but both did resistance to MEPM or CL, when determined by using a microdilution method. Whole genome sequence analyses revealed that the K. pneumoniae isolate harbored blCTX-M-55, blaTEM-1 and blashv-11 but not any carbapenemase-encoding genes, and that the E. cloacae did blatem-1, blashv-12 and blaatc-2 but not any carbapenemase-encoding genes. The CL-heteroresistant E. cloacae isolate had mutations in encoding genes of two-component systems (pmrABC and phoPQ) associated with CL resistance.

Conclusion: This is the first identification of MEPM-heteroresistant K. pneumoniae and CL-heteroresistant E. cloacae in Japan.