27th ECCMID Vienna, Austria 22 – 25 April 2017
The congress of ESCMID

Session: OS055 The complex epidemiology of carbapenemases

Category: 3b. Resistance surveillance & epidemiology: Gram-negatives

23 April 2017, 09:24 - 09:34
OS0291

Ability of blaNDM to disseminate worldwide into extensively drug-resistant bacterial hosts poses a major challenge to infection control and treatment: a global multi-centred whole-genome sequencing analysis

Oon Tek Ng*[1], Jia Jun Lee[2], Patrick Harris[3], Hanna Evelina Sidjabat[4], Hosam Zowawi[5], Giri Shan Rajahram[6], Ahneez Bt Abdul Hameed[6], Jayaram Menon[6], Fennie Kah Ling Fong[6], Katie Hopkins[7], David Wareham[8], Pak-Leung Ho[9], Stephanie Lo[9], Andes Lau[9], Rie Isozumi[10], Robin Patel[11], Scott A Cunningham[11], Shawn Vasoo[12], Milan Kojic[13], Wei Xin Khong[2]

[1]*Tan Tock Seng Hospital; Infectious Disease*

[2]*Tan Tock Seng Hospital*

[3]*Uq Centre for Clinical Research; Pathology Queensland*

[4]*The University of Queensland; Centre for Clinical Research*

[5]*Royal Brisbane and Women's Hospital, Uq Centre for Clinical Research; Infection and Immunity Theme*

[6]*Hospital Queen Elizabeth*

[7]*Public Health England*

[8]*Blizard Institute*

[9]*University of Hong Kong*

[10]*Osaka City University*

[11]*Mayo Clinic; Department of Laboratory Medicine and Pathology, Division of Clinical Microbiology*

[12]*Institute of Infectious Diseases and Epidemiology, Tan Tock Seng Hospital*

[13]*University of Belgrade, Institute of Molecular Genetics and Genetic Engineering*

Background: New Delhi metallo-β-lactamase genes (*bla*$_{NDM}$), are found in diverse Gram-negative bacterial strains. While tracking spread of bacterial clones has revolutionised infection control of many drug-resistant bacteria (e.g, MRSA, VRE, Mtb), deciphering spread of *bla*$_{NDM}$ is complicated by two additional tiers of gene spread: inter-plasmid gene module transposition and inter-bacterial plasmid conjugation.

Material/methods: To discern *bla*$_{NDM}$ transmission pathways to inform infection control, *bla*$_{NDM}$-positive isolates were collected worldwide (19 study sites in China, Czech Republic, India, United Kingdom, Malaysia, Oman, Pakistan, Qatar, Saudi Arabia, United Arab Emirates, United States, Vietnam and Singapore) over 5.3 years (December 2009 to April 2015). Whole genome sequences of the *bla*$_{NDM}$ isolates (N=473) were analyzed for genomic species, plasmid groupings and resistomes. Genomic transmission clusters were defined with a single nucleotide polymorphism (SNP) threshold based on pairwise Hamming distances (E. coli: 78 SNPs, K. pneumoniae: 118 SNPs).

Results: The majority of isolates were collected from Singapore (N=368, 78%) while the remaining were isolates from 12 other countries in Asia (N=56, 11.8%), Europe (N=35, 7.4%), the Middle East (N=13, 2.8%) and North America (1, 0.2%). Out of the 473 *bla*$_{NDM}$-positive isolates, 467 (98.7%) had a human origin, while 6 (1.3%) had an environmental origin. The main *Enterobacteriaceae* were *K. pneumoniae* (N=178, 37.6%), *E. coli* (N=147, 31.1%) and *E. cloacae* (N=62, 13.1%). One hundred and twenty-eight unique sequence types (STs) were identified amongst the Enterobacteriaceae. Bacterial strain type (STs) were diverse, though international 'high-risk' clones *E. coli* ST131 (N=17, 3.4%), *K. pneumoniae* ST147 (N=16, 3,4%) and *K. pneumoniae* ST11 (N=12, 2.5%) were the commonest STs. Of all plasmid incompatibility groups detected, IncFI (N=332, 70.2%) was most predominant. The colistin-resistance conferring gene, mcr-1, was detected in 7 isolates (6 from Singapore and 1 from China). Resistome analysis showed that 452 isolates (95.6%) carried at least one non-NDM β-lactamase gene. Additionally, most isolates carried at least one gene conferring resistance to aminoglycosides (N=426, 90.1%), fluoroquinolones (N=300, 63.4%), trimethoprim (N=329, 70%), sulfonamides (N=368, 77.8%), macrolides (N=236, 49.9%), phenicol (N=294, 62.2%), fosfomycin (N=237, 50.1%), and tetracyclines (N=266, 56.2%). In total, 17 genetic clusters involving 68 isolates were identified. All 17 genetic clusters were limited to Singapore and no international transmission cluster was detected.

Conclusions: Globally, *bla*$_{NDM}$ genes disseminate in diverse bacterial species with no predominant bacterial clones, suggesting that *bla*$_{NDM}$ can exploit multiple gene dissemination pathways. The complex genetic pathways of *bla*$_{NDM}$ spread poses a major challenge to infection control and therapeutic efforts worldwide.