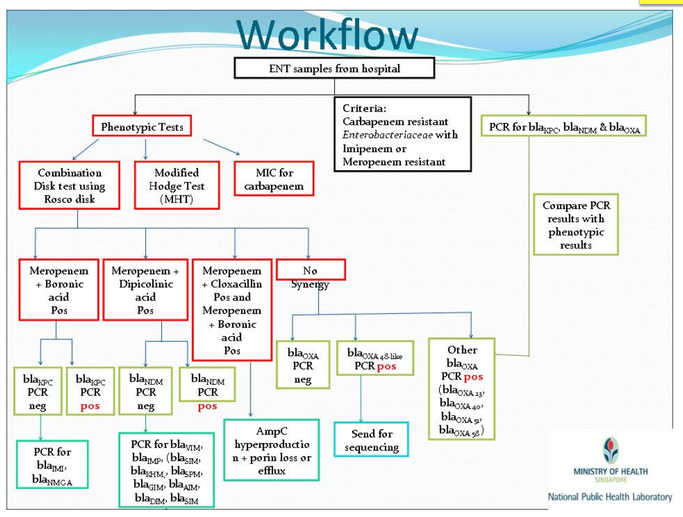
Changing trends in Carbapenemase - Producing Enterobacteriaceae in Singapore from 2010 to 2014

Prabha U. Krishnan[1,2], My Van La[2], Roland Jureen[2,3], Michelle Koh[2], Jeanette Teo[2,3], Raymond Lin[2,3].
[1] Tan Tock Seng Hospital, Singapore, Singapore. [2] National Public Health Laboratory, Singapore, Singapore. [3] National University Hospital, Singapore

Objectives: Carbapenemas Producing Enterobacteriaceae (CPE) pose a serious clinical challenge due to their high transmissibility and limited treatment options and have emerged as a public health threat in many countries around the world. We studied national trends in the CPE isolated in this city-state from its emergence in 2010 till August 2014

Methods: CPE isolates received at the National Public Health Laboratory (NPHL) from public hospitals, a few private hospitals and a community-hospital survey (done in 2013) were analyzed for their resistance mechanisms. A series of phenotypic tests were done for confirmation of the presence of carbapenemase enzymes; carbapenem encoding genes were determined using a reflex testing protocol of multiplex PCR reactions. The results obtained were analyzed for this study

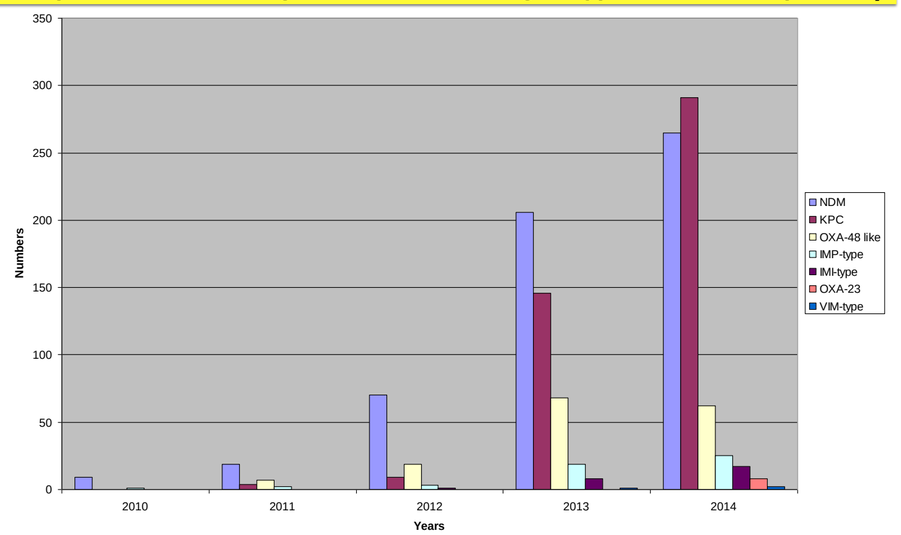


Results: Over this period 1230 CPEs were identified, with 2.5% of isolates harbouring dual carbapenemase encoding genes; *bla* NDM (New Delhi metallo-betalactamase) accounted for 46.4%, blaKPC (*Klebsiella pneumoniae* carbapenamase) for 38.8% and *bla*OXA 48-like (oxacillinase) for 13.5 %; other genotypes identified include *bla*IMP-like in 4.4%, *bla*OXA-23 in 0.7% and *bla*VIM in 0.2%. Both the NDM gene and the KPC gene were found predominantly in *Klebsiella pneumoniae* (40.5 and 51.7% respectively), *Escherichia coli* (29.3% and 26.9%) and *Enterobacter cloacae* complex (13% and 15%). These two genes started appearing in Citrobacter species in 2012 in Singapore, with NDM-Citrobacter accounting for 10.5 % of all NDM-CPE in 2013 – 2014. The OXA-48 like complex* included 55.8% OXA-181, 24.6% OXA 48 and 19.6% OXA 232; 76% of these were identified in *Klebsiella pneumoniae*

Carbapenemase Producing Enterobacteriaceae species 2010 - 2014

Year/Month	Sep - Dec 2010	2011	2012	2013	2014
Organism					
Cedecea species	**0**	**0**	**0**	**0**	**1**
Citrobacter species	**0**	**0**	**9**	**31**	**49**
Enterobacter aerogenes	**0**	**0**	**1**	**8**	**6**
*Enterobacter cloacae*complex	**1**	**6**	**12**	**67**	**107**
Escherichia coli	**4**	**6**	**27**	**107**	**196**
Klebsiella oxytoca	**0**	**0**	**0**	**7**	**8**
Klebsiella pneumoniae	**5**	**19**	**49**	**218**	**273**
Kluyvera georgiana	**0**	**0**	**0**	**2**	**0**
Morganella morganii	**0**	**0**	**0**	**0**	**3**
Proteus mirabilis	**0**	**0**	**0**	**1**	**4**
Providencia rettgeri	**0**	**0**	**1**	**0**	**0**
Serratia marcescens	**0**	**1**	**0**	**0**	**1**
Total	**10**	**32**	**99**	**441**	**648**

Carbapenemase Producing Enterobacteriaceae genotypes 2010 – 2014 (n= 1283)



Conclusions: The increase in numbers and species of CPE as well as the increase in types of carbapenemase encoding genes detected in this city-state are causes for concern and will have to be monitored closely. Because of the difficulty of detecting some of these CPE in routine diagnostic laboratories, it is likely that their prevalence is under-reported in most hospitals. There is an urgent need to develop effective and inexpensive diagnostic tests that can be incorporated into the routine laboratory workflow. Further epidemiological and detailed genetic studies could assist in understanding the subtle mechanisms of spread and help determine methods of preventing dissemination of these difficult-to-manage multi-drug resistant bacteria.

Acknowledgment: We acknowledge the microbiology laboratories at all participating hospitals for contribution of bacterial isolates to NPHL

MINISTRY OF HEALTH SINGAPORE
National Public Health Laboratory

Tan Tock Seng HOSPITAL