

Description of *bla*_{IMP-8} Producers in Enterobacteriaceae from Argentina

Author Block D. De Belder¹, E. Albornoz¹, M. Rapoport¹, D. Faccione¹, A. Togneri², M. Perez², F. Pasteran¹, A. MBL-Group¹, A. Corso¹, S. Gómez¹; ¹Natl. Reference Lab. in Antimicrobial Resistance (NRLAR) INEI-ANLIS-Malbrán, Buenos Aires, Argentina, ²HIGA Evita Lanús, Buenos Aires, Argentina

Abstract:

Background: The emergence of metallo- β -lactamases (MBL) of the IMP-type was reported in *Enterobacteriaceae* (ETB) in Argentina in 2008. Since then, they continued to be dispersed. Here, we describe the epidemiology of 40 IMP-producing clinical ETB.

Methods: MBL was suspected in 199 out of 1689 isolates received at the NRLAR between 2008-april 2016 due to ≤ 21 mm imipenem (IMP) inhibition halos. MBLs were screened with synergy between a carbapenem disk and EDTA/SMA, Triton Hodge Test, Blue Carba Test and Carba-NP-Direct tests. Susceptibility was studied by disc diffusion (CLSI). Extended-Spectrum β -Lactamases (ESBL) was suspected by No Susceptibility (NS) (intermediate+resistant) to aztreonam (ATM) and/or by the synergism between clavulanic acid and ATM. Mutations in Quinolone Resistance Determining Region (QRDR) were inferred due to no inhibition halos to nalidixic acid (NAL). Clonal relatedness was evaluated by XbaI-PFGE. Conjugation was studied with *E. coli*J53 sodium azide resistant. Resistant genes, alleles and genetic environment were studied by PCR and sequencing.

Results: *imp-8* was confirmed in 40/199 isolates. The remaining genes were: *ndm* (n=145) and *vim* (n=14). Species distribution was (n, %): *K. pneumoniae* (17, 42%); *E. cloacae* (12, 30%); *C. freundii* (3, 7.5%); *E. coli* and *C. farmerii* (2, 5% each); *S. marcescens*, *R. ornithinolytica*, *K. oxytoca* and *E. aerogenes* (1, 2.5% each). The isolation site was blood (58%), urine (10%), rectal swab (10%) and others (22%). IMP-8 isolates came from 12 hospitals, 24 (60%) from a single hospital. The cumulative n° of hospital/year was: 1/2008; 1/2010; 1/2011; 2/2013; 5/2014; 10/2015 and 12/April 2016. NS resulted: 97% to IMP, 88% to meropenem and 30% to ATM. NS to other drugs was: 73% NAL, 65% gentamicin, 60% CIP, 18% minocycline, 10% amikacin, 2.5% tigecycline and colistin. ESBLs were confirmed in 9/15: 7 *per*, 2 *ctx-m*, 9 others. Mutations in QRDR were inferred in 9/31. Plasmid mediated quinolone resistance (PMQR) mechanisms (*qnr* and *aac(6')Ib-cr*) was detected in 31 (77,5%): *qnrB*, *qnrS* and/or *aac(6')Ib-cr*. Only 20/31 with PMQR were categorized as CIP NS. No clonal relatedness was observed between *E. cloacae* and *K. pneumoniae* isolates. *bla*_{IMP-8} transconjugants were obtained in 6/6 *E. cloacae* and 1/2 *C. farmerii*.

Conclusion: Here, we alert of the emergence of IMP-8 in 9 species. Interestingly, CIP resistance was mainly due to PMQR. Moreover, our results suggest horizontal dissemination of *bla*_{IMP-8}