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ESBL and carbapenemase producers isolated from bacteraemia in patients with cancer and stem-cell transplant: data from the first multicentre study in Argentina

Fernando Pasteran*[1], Alberto Carena[2], Melina Rapoport[1], Mariela Soledad Zárate[3], Marta Giovanakis[4], Rosana Padlog[5], Graciela Greco[6], María Cristina García Damiano[7], Mario Vilaro[8], Maria Laura Chaves[9], Marcelo Bronzi[10], Sandra Valle[11], Fabian Herrera[3], Alejandra Corso[1]

[1]*Laboratorio Nacional de Referencia En Antimicrobianos, Inei-Anlis Dr. Carlos Malbran*

[2]*Cemic; Infectious Diseases*

[3]*Centro de Educación Médica e Investigaciones Clínicas, Cemic*

[4]*Hospital Britanico*

[5]*Hospital Higa San Martín*

[6]*Hospital Italiano de Buenos Aires*

[7]*Fundaleu*

[8]*Hospital Privado Centro Medico de Cordoba*

[9]*Hospital Municipal de Oncologia Marie Curie*

[10]*Instituto de Oncología Angel H. Roffo*

[11]*Instituto Alexander Fleming*

Background: The clinical and microbiological characteristics of bacteremia in cancer and Stem Cell Transplant (SCT) patients can be different depending on the site of onset and acquisition of the infection. The objective of this study was to characterize the ESBL and carbapenemase-producing

Enterobacteriaceae, *Pseudomonas aeruginosa* (PAE) and *Acinetobacter* spp. (ACI) isolated from episodes of bacteremia in adult patients with cancer and SCT.

Material/methods: Prospective, multicenter study. Episodes of bacteremia in adults patients with cancer and SCT were included in 10 centers of Argentina, from May 2014 to July 2016. Susceptibility profile of the isolates was determined according to CLSI standards. A subset of strains with non-susceptibility to extended spectrum cephalosporins (ESC) and/or carbapenems were further submitted to the NRL for molecular characterization of *bla* genes by PCR. Bacteria identification was confirmed using MALDI-TOF (Bruker). *pilV* gene was evaluated by PCR as a subrogate marker of *K. pneumoniae* (KPN) belonging to ST258. *mcr*-1 gene was evaluated by PCR.

Results: Of 585 episodes of bacteremia included, 185 were due to multidrug resistant GNB, being the most frequent extended spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae (44%) followed by carbapenemase-producing Enterobacteriaceae (18%), multidrug resistant PAE (11%) and multidrug resistant ACI (10%). A total of 63 isolates were selected for molecular characterization: 43 KPN, 7 E. coli (ECO), 3 E. cloacae (ECL), 6 PAE and 4 ACI. 34/53 Enterobacteriaceae displayed carbapenem resistance and were confirmed as: 22/34 KPC (20 KPN, 1 ECO, 1 ECL, among 8/10 Centers), 11/34 OXA-48-like (only KPN, among 4/10 centers) and 1/34 ECO dual producer of KPC+OXA-48-like. All OXA-48-like were confirmed as OXA-163. 6/11 OXA-163 co-produced ESBLs. 20/20 KPN KPC producers were not related to ST258. 4/53 Enterobacteriaceae were colistin resistant (KPN KPC) and tested negative for *mcr*-1 gene. 19/53 Enterobacteriaceae were resistant to ESC (12 KPN, 5 ECO, 2 ECL) and were confirmed as: 17 /19 ESBL producers and 2/19 (ECO) harbored plasmidic-AmpC (DHA-1). ESBL were confirmed as: 11/17 CTXM-1/15 (7 KPN, 2 ECO, 2 ECL), 1/17 CTXM-2 (ECO), 1/17 CTX-M-14 (ECO), 2/17 CTX-M unassigned group (ECO, KPN), 2/17 SHV-like (KPN). 6 PAE were carbapenemase producers: 4/6 KPC (1 Center) and 2/6 VIM producers (2 Centers). 4 ACI were carbapenemase producers (OXA-23, 2 Centers).

Conclusions: The most frequent carbapenemase in this patient population was KPC, mainly disseminated by non-ST258 KPN. Outstanding, one third of carbapenemase producers belonged to the OXA-48 group, larger than the general inpatient national population were the relative proportion of KPC/OXA-48 is about 32:1 ($p < 0.05$). The most frequent ESBL in this patient population was CTXM-1/15, in accordance with general inpatient national population. These findings must be taken into account when choosing the empirical treatment.