#P0410

ESBL AND CARBAPENEMASE PRODUCERS ISOLATED FROM BACTEREMIA IN PATIENTS WITH CANCER AND STEM-CELL TRANSPLANT: DATA FROM THE FIRST MULTICENTER STUDY IN ARGENTINA

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BACKGROUND & OBJECTIVE

The microbiological characteristics of bacteremia in cancer and Stem Cell Transplant (SCT) patients may differ according to the area of the world.

The **OBJECTIVE** of this study was to characterize:

I) the extended-spectrum β-lactamases (ESBL) and plasmidic AmpC in Enterobacteriaceae (ETB) and,

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

MATERIALS & METHODS

✓ A prospective, multicenter study. Episodes of bacteremia in adult patients with cancer and SCT were enrolled in 10 centers of Argentina, from May 2014 to July 2016.

✓ Susceptibility profile of the isolates was determined by disc diffusion and/or MIC (Liofilchem® gradient strips) according to CLSI standards.

✓ A subset of gram negative bacilli with non-susceptibility to extended spectrum cephalosporins (ESC) and/or carbapenems were further submitted to the National Reference Laboratory in Antimicrobial Resistance (NRL) for molecular characterization of *bla* genes by PCR.

✓ Bacteria identification was confirmed using MALDI-TOF (Bruker).

✓ Xba-I PFGE was determined for *K. pneumoniae* (KPN) isolates.

✓ *-pilV* gene of KPN was evaluated by PCR as a subrogate marker belonging to ST258 (Adler A. DMID 2014; Gomez S. IGE 2016).

✓ *mcr*-1 gene was evaluated by PCR.

RESULTS

*** Of 585 episodes of bacteremia included, 357 (61%) were from patients with hematological tumor, 124 (21.2%) with stem cell transplant and 104 (17.8%) with solid tumor.**

*** Gram-negative bacilli (GNB) were isolated in 387 episodes (66.2%), and gram-positive cocci in 211 (36.1%), being the most frequent: *E. coli* (ECO) (21.7%), *Klebsiella* spp. (20.9%), coagulase-negative staphylococci (CoNS) (13%), *Staphylococcus aureus* (10.4%) and *P. aeruginosa* (8.4%)**

*** Multi Drug Resistance (MDR) was observed in 261 isolates (44.6%)**
- **ESBL producing ETB: 31.4%**
- **MDR CoNS: 20.3%**
- **KPC-producing ETB: 12.6%**
- **MRSA: 8.8%**
- **MDR PAE: 8%**
- **MDR ACI: 7%**
- **Others: 11.9%**

*** A total of 63 MDR GNB were selected for molecular characterization:**
1) 19 ETB with ESCresistance: 17 with ESBL phenotype and 2 with plasmidic AmpC phenotype.
2) 34 carbapenem resistant ETB.
3) 6 high-level carbapenem resistance PAE (IMP and/or MER MIC >128µg/ml).
4) 4 carbapenem resistant ACI.

1. Extended Spectrum Cephalosporin resistance (ECS) in Enterobacteriaceae

19 ETB displayed ESC resistance

(12 KPN, 5 ECO, 2 *E. cloacae* - ECL).

17/19 isolates produced ESBLs:

15 CTX-M and 2 SHV-like. The remaining 2 isolates harboured DHA-1-plasmidic-AmpC (KPN)

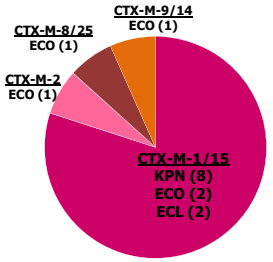


Fig. CTX-M variants and species

2. Carbapenemases in Enterobacteriaceae (N=34)

KPC was the most frequent carbapenemase in 23/34 isolates (67.6%), followed by OXA-48-like (OXA-163) in 11/34 isolates (32.3%)

- 20 KPC-producing KPN belonged to 15 different clonal types by *Xba*-I PFGE (6/20 isolates were clonally related, clone A - 1 Center), however **none of them belonged to the hyper-epidemic sequence type 258 clone**. Accordingly, all 20 KPC-producing KPN tested negative for *pilV* gene. These isolates belonged to 8 out of 10 centers.

- All 11 OXA-163 producers were KPN and belonged to 4 centers. 6/11 OXA-163 KPN co-produced ESBLs (CTX-M-2 and CTX-M-1/15).

- 4 ETB were colistin resistant (KPN KPC) but tested negative for *mcr*-1 gene.

Fig. Carbapenemases and species

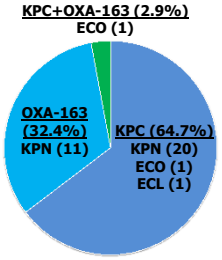
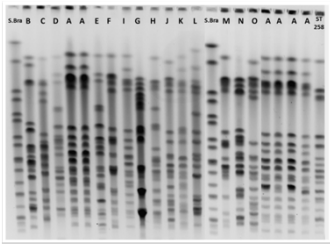


Fig. **KPC-producing KPN – XbaI** PFGE



S. Bra: Molecular size standard, Salmonella serotype Braenderup H9812 restricted with XbaI.
ST258: Representative profile of *K. pneumoniae* ST258 restricted with XbaI.

3 and 4. Carbapenemases in *P. aeruginosa* and *Acinetobacter baumannii*.

All 6 *Pseudomonas aeruginosa* were carbapenemase producers:
4 **KPC** (1 center), 2 **VIM** producers (2 centers).

All 4 *Acinetobacter baumannii* were carbapenemase producers: **OXA-23** (2 centers).

CONCLUDING REMARKS

- The most frequent ESBL in this patient population was **CTXM-1/15**, in accordance with general inpatient national population.

- The most frequent carbapenemase in this patient population was **KPC**, mainly disseminated by **non-ST258 KPN**.

- Remarkably, one third of carbapenemase producers belonged to the **OXA-48 group (OXA-163)**, a larger amount than the general inpatient national population where the relative proportion of KPC/OXA-163 is about 32:1 ($p < 0.05$).

- These findings must be taken into account when choosing the empirical treatment.

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