

# **TITLE:** EMERGENCY OF VANCOMYCIN-RESISTANT ENTEROCOCCI IN NATAL-BRAZIL

**AUTHORS:** Oliveira, E. S. de<sup>1</sup>; Novais, C.<sup>2</sup>; Freitas, A. R.<sup>2</sup>; Peixe, L.<sup>2</sup>; Melo, M. C. N.<sup>1</sup>

**INSTITUTION:** <sup>1</sup>Universidade Federal Rio Grande do Norte - Departamento de Microbiologia e Parasitologia - Laboratório de Bacteriologia Médica – Campus Universitário Lagoa Nova, CEP 59078-970 - Natal/RN – Brazil. Phone: +55 84 3215-3437; <sup>2</sup>Universidade do Porto – Faculdade de Farmácia – Departamento de Ciências Biológicas- Rua Jorge Viterbo Ferreira nº 228 - 4050-313 - Phone: +351 22042-8588 – Porto-Portugal.

## **ABSTRACT:**

Vancomycin-resistant enterococci (VRE) clonal spread and outbreaks cause major problems in health institutions around the world. In Brazil, several available studies describe VRE outbreaks or clonal dissemination scenarios mostly involving *Enterococcus faecalis* and *Enterococcus faecium*. However, any VRE was reported until this moment in Natal, northeast of Brazil. We characterize, at molecular level, sixty-two VRE isolates from surveillance culture and others clinical specimens collected from 51 patients of 7 hospitals, for two years (2015-2016). Identification at the species level was performed by automated system VITEK 2 and confirmed by PCR (*sodA* and *ddl* genes). Susceptibility to 9 antibiotics was assessed by disk-difusion, E-test (vancomycin), broth-microdilution (linezolid), agar dilution (teicoplanin). Search of vancomycin resistance (*vanA/vanB*) and putative virulence (*cyl/asa/gel/esp*) genes was performed by PCR. Clonal relationship was evaluated by Pulse-field Gel Electrophoresis (PFGE), and representative strains from main PFGE types also by Multilocus Sequence Typing (MLST). Sixty-one isolates were identified as *Enterococcus faecalis* and only one as *Enterococcus faecium*. Resistance to vancomycin, teicoplanin, ciprofloxacin, tetracycline and erythromycin were observed in all isolates. Vancomycin and teicoplanin MICs were 16 to  $\geq 256$   $\mu\text{g/ml}$  and 4 to 64  $\mu\text{g/L}$ , respectively. In addition, 88,7% (n=55) and 40,3% (n=25) isolates were also resistant to gentamicin or streptomycin, respectively. None was resistant to linezolid or chloramphenicol. Just the *E. faecium* was ampicillin resistant. Operon *vanA* was observed in all isolates. Occurrence of *E. faecalis* virulence factors included *gelE* (98,4%; n=60), *asa1* (100%; n=61), *cylA* (16,4%; n=10) and *esp* (9,8%; n=6). Two PFGE types were identified; type A (50,8%; n=31) and type B (49,18%; n=30). The MLSTs of the representative isolates were typed as ST525 and ST6. Both clones were co-circulating during the period of the study. This study highlights a high rate of patient colonization with vancomycin-resistant *E. faecalis* with *vanA* and a silent spread of two clones previously associated with human infections in Brazil (ST525) or worldwide (ST6). Although their transmission routes of this ERV in Natal remain to clarify, the inter-hospital spread during a long period of time highlight the need of preventions measures to contain a potential ERV infection epidemic scenario.

**Keywords:** VRE; clonal spread; surveillance culture; PFGE; MLST.

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