

TITLE: RISK FACTORS AND PREDICTORS OF MORTALITY IN PATIENTS INFECTED BY MULTIDRUG-RESISTANT GRAM-NEGATIVE BACTERIA IN INTENSIVE CARE UNIT

AUTHORS: DEGLMANN, R.C.; KOBBS, V.C.; LIMA, H.; FRANÇA, P.H.C.

INSTITUTION: UNIVERSIDADE DA REGIÃO DE JOINVILLE – UNIVILLE, JOINVILLE, SC (RUA PAULO MALSCHITZKI, 10, CAMPUS UNIVERSITÁRIO, ZONA INDUSTRIAL NORTE, CEP 89219-710, JOINVILLE – SC, BRAZIL).

ABSTRACT:

Infections by multidrug-resistant (MDR) Gram-negative bacilli increase risk of mortality of patients. Our aim was to investigate the risk factors for acquiring healthcare-associated infections (HAI) by multidrug-resistant Gram-negative bacilli (MDR-GNB) and the predictors of mortality in patients admitted to the intensive care unit (ICU). It was an observational, comparative and prospective study, employing the medical records of patients (≥ 18 years old) admitted to the ICU of a public hospital, in Southern Brazil, between January 1, 2016 and December 31, 2017, with ≥ 48 hours of length stay. Patients with HAI were stratified as infection by MDR-GNB or non-MDR-GNB. The variables of interest included clinical data, comorbidities, resistance pattern of the isolates and antimicrobial treatment (ATM). Molecular investigation for carbapenemase was by polymerase chain reaction. Data were analyzed by logistic regression using univariate and multivariate models, being considered as significant when $p \leq 0.05$ and $p \leq 0.200$, respectively. During the study, 2,124 patients were admitted to the ICU, while 330 had HAI and were effectively included. Most of cases (176; 69%) were confirmed as GNB infected, and these were distributed as MDR-GNB (45.5%) and non-MDR-GNB (54.5%). There were no significant differences for gender (males = 67%; $p = 0.673$) and age (median = 65 years old; $p = 0.684$), between groups. The significant risk factors for acquisition of HAI by MDR-GNB were hospitalization stay longer than 4 days prior admission to the ICU ($p = 0.017$) and use of ATM in the ICU prior to HAI diagnosis ($p = 0.043$). The MDR-GNB group was exposed to carbapenems (41%), piperacillin/tazobactam (38%), 4th generation cephalosporins (29.5%), ampicillin/sulbactam (19.7%), and fluoroquinolones (11.4%). *Klebsiella pneumoniae* (38.8%) and *Acinetobacter calcoaceticus* - *A. baumannii* Complex (ACB; 36.3%) were predominant among MDR-GNB, and *Pseudomonas aeruginosa* (32.3%) and *K. pneumoniae* (17.7%) among non-MDR-GNB, characterizing a significant difference ($p < 0.001$) between groups. The presence of MDR-GNB was a significant predictor for mortality ($p = 0.005$). Among patients who died, 86.6% of the ABC isolates were positive for *bla*_{OXA51} and *bla*_{OXA23} genes, as well as 65.8% of *K. pneumoniae* strains showed *bla*_{KPC} gene. In conclusion, the rational use of ATM is important considering the limited therapeutic options and the association of MDR-GNB infections with mortality among patients in ICU.

Key-words: healthcare-associated infections, multidrug-resistant bacteria, carbapenem resistance

Development Agency: Research Support Fund from the Universidade da Região de Joinville (FAP/UNIVILLE) and Support Fund for the Maintenance and Development of Higher Education in Santa Catarina (FUMDES/SC).