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The impact of antimicrobial resistance on clinical outcomes: results of the Italian SPIN-UTI network

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Background: Antimicrobial resistance (AMR) is a global public health threat and healthcare-associated infections (HAIs) caused by resistant bacteria have been associated with severe adverse outcomes, such as higher mortality, longer hospital length of stay and increased costs, especially in Intensive Care Units (ICUs). It has been recently shown that HAIs represent the most significant burden among infectious diseases in Europe. However, the fraction of the burden of HAIs attributable to AMR is currently unknown and is expected to vary because of the large intercountry differences in

antimicrobial resistance percentages. The main aim of the present study was to investigate the impact of HAI and of AMR on mortality and length of ICU stay, focusing on multidrug-resistant (MDR) *Acinetobacter baumannii* and *Klebsiella pneumoniae* HAIs in Italy.

Material/methods: The study was conducted in the framework of the "Italian Nosocomial Infections Surveillance in Intensive Care Units (ICUs) network" (SPIN-UTI) of the GISIO-Sitl. Data were prospectively collected from ICUs during the period 2006-2015 using the patient-based European protocol for surveillance of HAIs in ICU (ECDC HAI-Net ICU protocol). An isolate was defined MDR if was non-susceptible to at least 1 agent in ≥ 3 antimicrobial categories. The risk of death was estimated using Cox regression analysis.

Results: Of the 13103 patients enrolled by the 79 participating ICUs, 1764 had an ICU-acquired infection (13.5% of patients). The risk of death was significantly higher for infected patients compared with the rest of the cohort (RR: 2.5 CI95%: 2.3-2.7). After Cox regression analysis, different factors, including SAPS II score above the median value (HR: 3.1; 95%CI: 2.5-3.9), older age (HR: 1.5; 95%CI: 1.2-1.7) and type of admission (HR: 1.3; 95CI%: 1.1-1.7), were significantly associated to the risk of death, while the presence of HAI was not significantly associated to the risk of death. A total of 38.8% of patients were infected by *A. baumannii* and/or *K. pneumoniae* (co-infection: 5.8%). Particularly, among patients with *A. baumannii* infection, 95.5% had a MDR *A. baumannii* and among patients with *K. pneumoniae* infection, 70.8% had a MDR *K. pneumoniae*. Mean length of ICU stay was significantly higher in patients with MDR *A. baumannii* and/or *K. pneumoniae* infection than patients infected by other microorganisms (20.5 versus 16.7 days; $p < 0.001$). Using a Cox regression analysis, the presence of MDR *A. baumannii* and/or *K. pneumoniae* infection was significantly associated to the risk of death (HR: 1.3; 95%CI: 1.1-1.6).

Conclusions: The present study demonstrated the significant burden of HAI caused by MDR *A. baumannii* and *K. pneumoniae* strains, associated with higher mortality risk and length of ICU stay, highlighting the need for effective efforts to prevent and control these infections and minimize the impact of AMR in intensive care.