Isolation of clinical strains of *Staphylococcus epidermidis* from a Portuguese hospital and assessment of their relationship between biofilm formation capacity and antimicrobial resistance

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Staphylococcus epidermidis has been documented as an emergent pathogen responsible for many healthcare-associated infections (HAIs). These infections are an increasing cause of major concern not only due to the high distribution of methicillin resistance, but also due to their ability to form biofilm, which increases their persistence, impairs patient's quality of life and leads to failed treatment and extra costs. Portugal has one of highest incidence rates of HAIs in Europe. However, bacteriological information that may shed light on the clinical significance of *S. epidermidis* Portuguese isolates and provide data for control as well as epidemiological measures is missing. In order to fill this gap, the aim of this study was to isolate and determinate the antibiotic resistance profile of clinical strains of *S. epidermidis* and ensure its association with phenotypic and genotypic biofilm-associated determinants.

Of the 89 studied patients, 52 (58.4%) were men and the mean age was 45 years old. Bloodstream infections (69.7%) were the most frequently reported infections during the study period and almost a third of all infections were catheter-related. The majority (85.4%) of the clinical isolates were *mecA*-positive and among those, 92.1% were also resistant to 3 or more of the antimicrobial agent groups tested and hence considered multidrug-resistant (MDR). Resistance also reaches higher levels among β-lactam antibiotics (96.4%) and erythromycin (79.8%). Notwithstanding, positive associations were found between MDR and MRSE strains, between MDR strains and prescription of at least one antimicrobial agent and between patients under antibiotic therapeutic and MRSE strains. Regarding the phenotypic and molecular features, the majority (64%) of the clinical isolates were considered biofilm producers and all strong producers were carriers of the *icaA* gene, although equal distributed among MRSE and MSSE strains. The genetic combination most frequently observed was $icaA^{+}aap^{+}$ (41.6%) followed by $icaA^{+}aap^{+}bhp^{+}$ (21.3%). Additionally, strains with the genetic combination $icaA^{+}aap^{+}bhp^{+}$ were positively associated with both MRSE and MDR phenotype.

Our results confirmed the impact of *S. epidermidis* on hospital-acquired infections and highlight the burden of antimicrobial resistance, mainly multidrug resistance that reached alarming levels in this tertiary-care hospital. Moreover, this data raised concerns regarding antimicrobial strategies previously adopted. In addition, an association between the carriage of some virulent-associated genes and biofilm phenotype was clear, mainly regarding the carriage of *icaA* gene that demostrated to be essential in the biofilm process of *S. epidermidis* clinical strains.

Keywords: *Staphylococcus epidermidis*; antibiotic resistance; phenotypic and clinical features.