TITLE: CHARACTERIZATION OF METHICILLIN-RESISTANT *Staphylococcus aureus* ISOLATES OF THE MULTIRESISTANT AND EMERGENT LINEAGE USA100/ST5/SCC*mec* II IN RIO DE JANEIRO HOSPITALS

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ABSTRACT:

In the last years, BEC/SCC*mec*III/ST239 clone has been substituted by other clonal lineages, including the USA100/SCC*mec*II/ST5 lineage in Rio de Janeiro hospitals. These isolates are associated with multidrug resistance, mainly vancomycin and daptomycin that may be used as treatment of bloodstream infections (BSI) caused by methicillin-resistant *Staphylococcus aureus* (MRSA). Besides, they might produce biofilm, which is correlated with persistent infections. The objective of this study was to evaluate the biofilm formation, type and activity of *agr* operon, as well as, to characterize the resistance profile to oxacillin, vancomycin, and daptomycin of 28 USA100 MRSA isolates from BSI, between 2011 and 2015, from a teaching hospital of Rio de Janeiro. The ability to form biofilm was evaluated through a microtiter plate assay stained with 0.1% safranin. The type and presence of the *agr* operon was verified by a multiplex-PCR methodology, and its activity was analyzed by the δ-hemolysin expression in blood agar. The minimum inhibitory concentration (MIC) was determined through broth microdilution for oxacillin, vancomycin, and daptomycin. Most of the isolates (13; 46%) were moderate biofilm producers while strong, weak and non-biofilm production phenotypes were observed in 36% (10), 14% (4) and 4% (1) of the isolates, respectively. All of the 28 isolates had the *agr* operon type II. However, about 50% (14) of them had this operon non-functional. As expected, all of the isolates were resistant to oxacillin with most of them (15; 54%) presenting MIC ≥256 μg/mL. Three (11%) isolates presented a vancomycin-intermediate resistance phenotype, and 12 (43%) isolates were non-susceptible to daptomycin. Six of the 12 daptomycin non-susceptible isolates presented a non-functional *agr* operon. However, it was not found a correlation between biofilm production or non-susceptibility to daptomycin and activity of *agr* operon. Among the 12 daptomycin non-susceptible isolates, nine (75%) were moderate or strong biofilm producers, with one of these also vancomycin-intermediate resistant. These results highlight the importance of this lineage due to its capacity to become resistant to antibiotics and its ability to produce biofilm that may allow them to cause more serious infections. More studies are necessary to investigate the reason why half of the USA100 isolates do not have an *agr* operon active.

Keywords: *Staphylococcus aureus*, USA100, daptomycin, *agr*, biofilm

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