Background: Skin and soft tissue infections (SSTI) caused by *Staphylococcus aureus* represent a growing problem in Colombia due to the massive dissemination of a community-associated (CA) strain SAMR USA300 Latin American Variant. The aim of this study was to evaluate risk factors associated with complicated infection of Skin and Soft Tissue (CSSTIs) caused by CA-Methicillin-Resistant *Staphylococcus aureus* in Colombia.

Methods: We conducted a prospective cohort study with a nested case-control design in 13 hospitals in Colombia between January 2009 and June 2015. We included patients aged ≥18 years with CSSTI who required at least 48 hours of inpatient care or patients with hospital-acquired SSTI. Patients with osteoarticular infections, burns or viral infections were excluded. Case patients were defined as having an SAMR SSTI and control as those with SSTI caused by other microorganisms.

Results: A total of 1134 patients were included with 177 (15.6%) patients in which *Staphylococcus aureus* was isolated. Multivariate logistic regression identified the following risk factors for SAMR infection: abscesses [odds risk (OR) 2.54, 95% confidence interval (CI) 1.79 - 3.61], forunculosis [OR 3.79, 95% CI 1.04-13.85], age 18 - 44 years [OR 2.46, 95% CI 1.55-3.93], previous management in outpatient setting [OR 1.76, 95% CI 1.14 - 2.71] and history of bite [OR 1.98, 95% CI 1.08-3.62]. Of note, 57% patients received inappropriate therapy for SAMR.

Conclusion: CSSTIs caused by SAMR in Colombia mainly affect young patients and is often associated with abscesses. Previous management in outpatient settings is an important risk factor for SAMR acquisition. Although clinicians should consider SAMR when the initial empirical treatment for purulent SSTIs, there seems to be low awareness of this fact in Colombia.