Characterization of circulating clinical multi-drug resistant and methicillin resistant *Staphylococcus aureus* isolates in Peru

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134

INTRODUCTION

Staphylococcus aureus is one of the major threats to hospitalized patients given its ability to rapidly acquire resistance to multiple antibiotics. Indeed, *S. aureus* is in the High Priority list for research and development of new antibiotics declared by the World Health Organization [1].

Hospitalized individuals with longer lengths of admission have an increase of colonization by multidrug resistant and/or methicillin resistant *S. aureus* (MDR-SA and MRSA, respectively), which limits therapeutic options [2, 3].

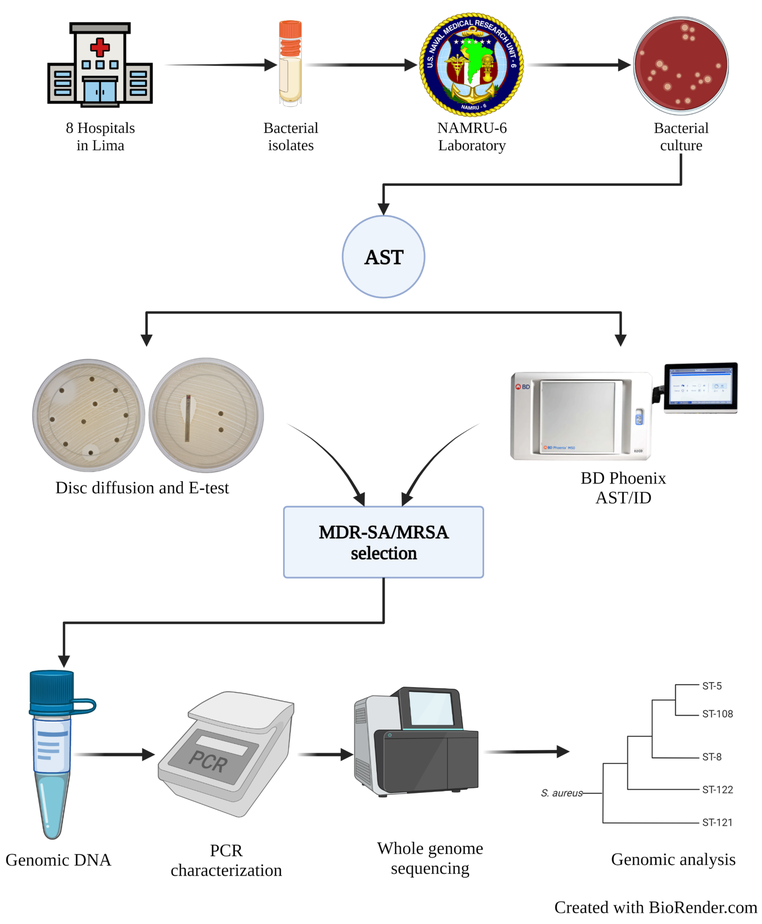
Dissemination of *S. aureus* clones in health-care settings is of high concern where over-the-counter use of antibiotics is widespread, and therefore antimicrobial susceptibility surveillance is necessary to identify trends in resistance. In addition, molecular surveillance is also of critical importance due to its inherent capability to provide an accurate description of the distribution of clinically important clonal *S. aureus* populations.

In Latin America, sequence type (ST) 5 clones have been associated with previous outbreaks [4], and it is currently one of the predominant clones present [5, 6].

Here we describe a four-year surveillance study of MDR-SA and MRSA in hospitals in Lima with further characterization by whole genome sequencing (WGS).

MATERIAL & METHODS

Bacterial isolates of nosocomial origin were prospectively collected between 2015 and 2018 from hospitalized patients from 8 hospitals in Lima, Peru. Sample's origin/type were categorized as: lower respiratory tract, upper respiratory tract, wound, blood, urinary tract, abdominal cavity, and rectal swabs. Bacterial isolates were transported from the hospital site to the NAMRU-6 laboratory and underwent further characterization, as follows:



RESULTS

We obtained 3103 bacterial pathogens from 8 different hospitals in Lima, of those 232 were identified as *S. aureus* from individuals between 2015 and 2018. We then selected 80/232 (35%) isolates that were resistant to ≥2 antibiotic classes and/or MRSA from for further characterization, of which 42.5% were obtained from the lower respiratory tract (Table 1).

Table 1. MDR-SA frequencies according to nosocomial origin.

Origin/type	Isolates	Frequency
Lower respiratory tract	34	42.5%
Upper respiratory tract	13	16.25%
Wounds	4	5%
Blood	17	21.25%
Urinary tract	2	2.5%
Abdominal cavity	5	6.25%
Rectal swab	5	6.25%
Total	**80**	**100%**

S. aureus isolates were resistant against nine different antimicrobial classes (Fig. 1). Of note, 79% (63/80) of MRSA isolates were also resistant to macrolides, quinolones, and lincomycins. Additionally, 81% (64/80) of the isolates had inducible resistance to clindamycin. Notably, 5% (4/77) of the MRSA isolates carried the Panton Valentine leucocidin gene *lukS* and the *mecA* gene, as revealed by multiplex PCR.

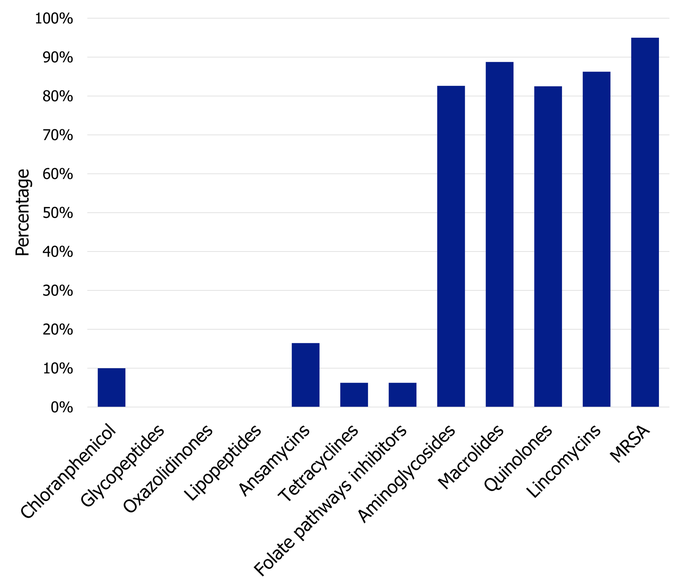


Figure 1. MDR-SA frequencies of resistance to different antibiotic classes.

WGS analysis of the *S. aureus* isolates revealed the presence of 26 genes associated with antimicrobial resistance (Fig. 2). *In silico* multilocus sequence typing (MLST) assigned the ST5 to 87.5% of the MRSA isolates (Fig. 3), while the remaining isolates were poorly represented among ST clusters. We also observed samples with multiple high related clusters, mainly among ST5 cluster, indicating the possibility of nosocomial dissemination and possible outbreak events.

RESULTS (Continued)

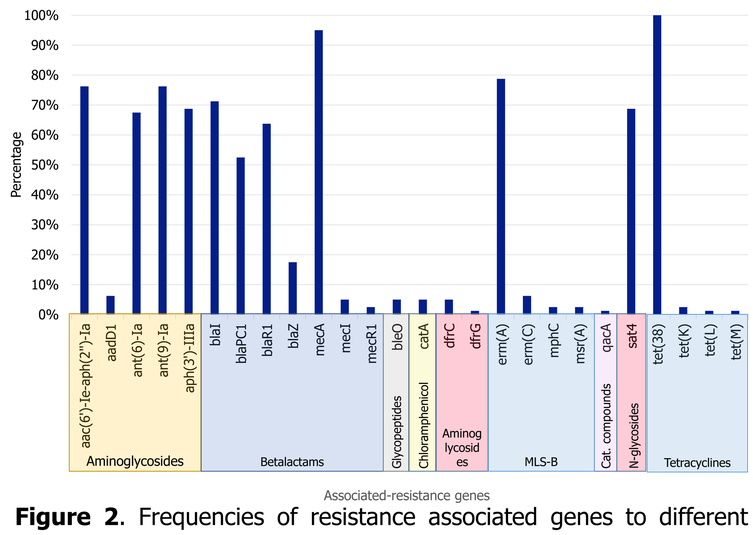


Figure 2. Frequencies of resistance associated genes to different antibiotic classes.

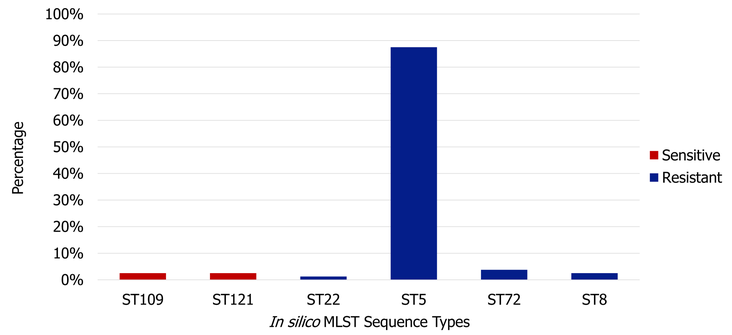


Figure 3. MRSA and non-MRSA distribution in ST clusters.

CONCLUSIONS

- Nearly 80% (63/80) of collected MRSA isolates were resistant to macrolides, quinolones, and lincomycins. Thus, due to the high levels of clindamycin resistance observed in MRSA isolates, it is highly recommended to include continuous surveillance of inducible clindamycin resistance.
- *In silico* MLST showed ST5 as the predominant cluster. Single nucleotide polymorphism analysis shed light upon the close relatedness among ST5 cluster, indicating potential nosocomial dissemination and outbreaks.
- Because of the high levels of resistance to multiple antimicrobials herein reported, as well as dissemination of ST5 clones not limited solely to regional spread, continued active surveillance of *S. aureus* is recommended to prevent antimicrobial therapy failure.

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