The changing pattern of methicillin-resistant *Staphylococcus aureus* clones in Latin America: implications for clinical practice in the region

ABSTRACT

Methicillin-resistant *Staphylococcus aureus* (MRSA) clones belonging to the Brazilian, Pediatric, Cordobes/Chilean and New York/Japan clonal complexes are widely distributed across Latin America, although their individual distribution patterns and resistance to antimicrobial drugs are constantly changing. Furthermore, clones with increased virulence are beginning to appear more frequently both in hospital and community settings, and there is evidence that virulence factors can be transferred between hospital- and community-associated clones through recombination. These changing patterns have significant implications for clinical practice in the region. Most importantly, clinicians need to be aware of the changing antimicrobial resistance profile of circulating MRSA clones in their region in order to choose the most appropriate empiric antimicrobial therapy. Thus, regional molecular epidemiology programs are required across the region to provide accurate identification and characterization of circulating MRSA clones.

Keywords: MRSA, clones, molecular epidemiology, Latin America.

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INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) poses a major threat to public health worldwide, due to the rapid spread and diversification of pandemic MRSA clones with increasing virulence and antimicrobial resistance. In Latin America, MRSA is a leading cause of nosocomial infections, and the prevalence of MRSA in community-acquired infections is growing.[1]

Although relatively few studies have addressed the molecular epidemiology of MRSA clones across Latin America, it is clear that several clones circulate in the region and that these differ in their virulence, antimicrobial resistance profile and geographical distribution.[1,2] Characterization of these clones is important if appropriate local treatment strategies are to be developed. For example, a thorough knowledge of clones circulating within a region may be used to assess the relationship between clonal types, disease symptoms, antibiotic choice and clinical outcomes. Furthermore, understanding why specific clones predominate in different regions of Latin America is an important and necessary step towards developing the most effective strategies for controlling the spread of MRSA in the region.

Here, we summarize current understanding of the spread of pandemic MRSA clones and highlight the distribution of major clones across Latin America, both in hospitals and in the community. Specific virulence factors and bacterial resistance patterns are highlighted, and their impact on clinical outcome is discussed.

EVOLUTION OF MRSA CLONES

Evolution of bacterial clones

Bacterial clones are genetically identical cells descended from a single common ancestor. Over time, members of a single clone may differentiate through point mutations, recombination, and the acquisition or deletion of mobile genetic elements. This differentiation provides additional means for the acquisition of pathogenic charac-

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teristics, such as antibiotic resistance. Thus, genetic variation gives rise to extensive genomic and phenotypic diversity.

Emergence of antibiotic resistant *S. aureus* clones

Clones of *S. aureus* have a history of antibiotic resistance that began within 4 years of the introduction of penicillin into clinical practice,[3] and by 1944, clones of *S. aureus* resistant to penicillin had been isolated. In the subsequent years, *S. aureus* became resistant to all of the natural penicillins.

MRSA was first reported in the early 1960s, shortly after the introduction of methicillin.[4] Early MRSA clones had similar genetic properties to the methicillin-susceptible *S. aureus* (MSSA) clones that were epidemic in Europe.[5] MRSA exhibits resistance to methicillin through a penicillin-binding protein encoded by the gene *mecA*, which was acquired by successful clones of MSSA from an unknown heterologous source. The *mecA* gene is carried by a mobile genetic element called the staphylococcal cassette chromosome *mec* (SCC*mec*). Multiple forms of SCC*mec* have arisen through the horizontal transfer of *mecA* in independent events, and, to date, seven main forms have been identified (I, II, III, IV, V, VI and VII).[6] All types of SCC*mec* confer resistance to -lactam antibiotics, and SCC*mec* types II and III provide resistance to multiple classes of antibiotics.[7]

During the evolution of MRSA clones, independent excision of SCC*mec* is a common phenomenon, resulting in the loss of methicillin-resistance and the transformation of a MRSA clone into a MSSA clone. Hence, clones may evolve from MSSA into MRSA, or from MRSA into MSSA, through the acquisition and excision of SCC*mec*, respectively.[8]

Several molecular typing methods are used routinely to characterize MRSA clones, including pulsed-field gel electrophoresis (PFGE), multilocus sequence typing (MLST) and SCC*mec* typing.[9] These methods have helped researchers to map the spread and evolutionary path of MRSA clones.[7,8]

MRSA has traditionally been regarded as a nosocomial pathogen,[10] but more recently, MRSA infections have appeared in community settings.[11] The clones typically responsible for hospital- and community-acquired MRSA infections have been classified as healthcare-associated MRSA (HA-MRSA) and community-associated MRSA (CA-MRSA), respectively.[12] These clones can be distinguished based on specific microbiologic and genetic characteristics, and often have different epidemiologic, clinical and therapeutic characteristics (Table 1).[10,11] Occasionally, hospital-acquired infections may be derived from CA-MRSA strains, and infections acquired in the community may carry healthcare-associated risk factors. Definitive HA-MRSA and CA-MRSA designations for individual clones, therefore, rely on microbiologic and genetic characterization, and the terms 'healthcare-acquired' and 'community-acquired' refer to the location at which the infection was acquired.[12]

International spread of MRSA clones

S. aureus clones spread quickly around the world,[13] disseminating efficiently between countries, within countries and in smaller geographic areas, and usually with concomitant evolution from a methicillin-sensitive to a methicillin-resistant phenotype.[5,14] Most nosocomial MRSA infections worldwide are derived from one of five major lineages known

Table 1. Common characteristics of infections caused by HA-MRSA and CA-MRSA

Characteristic	HA-MRSA	CA-MRSA
Year of discovery	1961	1980s
Population at risk	Patients having previous hospitalization, surgery, residence in long-term care facilities, dialysis, permanent indwelling catheters, intensive care unit	Children, homeless, men who have sex with men, athletes, military recruits, jail inmates, native Americans, Pacific Islanders, adult emergency department patients
Main clinical syndromes	Bacteremia, HAP, VAP, catheter- and prosthetic-related infections	SSTI, necrotizing CAP, bacteremia, osteomyelitis
Antibiotic resistance profile	Multidrug resistant; including β-lactams, macrolides, TMP-SMX, lincosamides, tetracyclines, rifampin, quinolones Growing resistance to glycopeptides also	Resistant to β-lactams. Variable susceptibility to macrolides, TMP-SMX, tetracyclines, lincosamydes
SCC*mec* type associated with strains causing infection	I, II and III	IV and V
Expression of PVL	Rare	Common

HAP: hospital-acquired pneumonia; VAP: ventilator-associated pneumonia; SSTI: skin and soft tissue infection; CAP: community-acquired pneumonia; TMP-SMX: trimethoprim-sulfamethoxazole; SCC*mec*: staphylococcal chromosomal cassette *mec*; PVL: Panton-Valentine leukocidin; PFGE: pulsed-field gel electrophoresis.

as clonal complexes (CC): 5, 8, 22, 30 and 45.[7,15,16] Between 1994 and 2000, surveillance data collected by the CEM/NET initiative identified five predominant pandemic clones (Brazilian, Iberian, Hungarian, pediatric and New York/Japan [NYJ]) within these clonal complexes, and these accounted for nearly 70% of MRSA isolates worldwide.[17]

The intercontinental spread of MRSA derived from a single ancestral MRSA clone was observed in the USA, UK, Denmark, Switzerland, Egypt and Uganda in the early 1990s. In the late 1990s, further spread was noted when MRSA clones previously isolated from Australia, US and Ireland, were found to have similarities with other MRSA clones collected around the world.[13,18]

Within countries, MRSA clones have disseminated rapidly and efficiently. Diversification and displacement of these clones is similarly rapid. Over a 9-year period in Spain, the common NYJ MRSA clone was displaced by the Brazilian MRSA clone, which was then displaced by the now-predominant EMRSA-16 clone.[19] Similarly, in Belgium, epidemic MRSA clones belonging to clonal complexes 5, 8, 22, 30 and 45 diversified rapidly, and by 2001, these clonal complexes showed broad geographic distribution in Belgian hospitals, in contrast to earlier survey results.[15] In Portugal, the predominant Brazilian MRSA clone was replaced in hospitals by two earlier MRSA clones over a 16-year period.[16]

In the USA, HA-MRSA clones are rapidly being replaced by CA-MRSA clones. The extent of this replacement varies between areas, but in one Chicago hospital the proportion of community-associated isolates increased from 24% to 49% over 3 years.[20]

MRSA CLONES IN LATIN AMERICA

Since the first report in 1994 of an autochthonous MRSA clone originating in Brazil,[21] known as the Brazilian clone, four additional clones circulating in Latin America have been described; the Cordobes, the Pediatric, the Chilean and the NYJ clones.[22-24] The closely-related Cordobes and Chilean clones are now considered to be a single clone (Cordobes/Chilean). All of these clones circulate extensively in the region (Figure 1[23-36]), and there is evidence supporting the appearance of genetic variants. Several minor clones have also been identified, although these currently occur in restricted geographic areas (Figure 1[23-36]).[37]

The Brazilian clone (ST239-SCC*mec* type III) has been isolated throughout Brazil and has extended into several other countries, including Argentina, Chile, Colombia, Ecuador, Paraguay, Peru and Uruguay. Several genetic variants have been identified, and together these are termed the Brazilian epidemic clonal complex (BECC).[26] The pathogenicity of the Brazilian clone derives from several properties, which are present to different degrees in different variants: multidrug resistance, including resistance to -lactams, chloramphenicol, quinolones, lincosamides, erythromycin, aminoglycosides and trimethoprim-sulfamethoxazole (TMP-SMX); resistance to mupirocin;[38] production of a protective biofilm;[26] ability to adhere to, and invade, airway epithelial cells;[26] and production of toxins, such as enterotoxins and Panton-Valentine leukocidin (PVL).[34]

Figure 1: MRSA clones circulating in Latin America identified since 2000[23-36]

MRSA Clones	MW2: MW2-related
Br: Brazilian and variants	NY/J: New York/Japan-related
C: Cordobes/Chilean	OSPC: Oceania Southwest Pacific
CM: CMRSA-6 (Canadian)	P: Pediatric-related
H: Hungarian	U: Uruguayan hospital
I: Iberian-related	UR6: Uruguayan community outbreak
M: Mexican	WA1: Western Australia 1

The Cordobes and Chilean clones (ST5-SCC*mec* type I) were identified separately in isolates from Argentina[23] and Chile,[22] and were later considered to be variants of the same clone. In Argentina, the Cordobes/Chilean clone has rapidly replaced the closely-related Brazilian clone, and it now predominates in several Latin American countries, including Argentina, Chile, Paraguay and Colombia,[27,32,35] where it is associated with nosocomial outbreaks. The Cordobes/Chilean clone shows a multidrug resistant phenotype, including resistance to erythromycin, although variants are still susceptible to glycopeptides, linezolid, TMP-SMX, rifampin and tetracyclines.

The pediatric (USA800; ST5-SCC*mec* type IV or SCC*mec* type VI) and NYJ (USA100; ST5-SCC*mec* type II) MRSA clones have also spread successfully through Latin America. Variants of the pediatric clone, with heterogeneous and low-level resistance to methicillin and resistance to b-lactam antimicrobials, have caused infections in Brazil, Argentina and Colombia,[23,30,39] and have developed multidrug resistance in some hospitals in Latin America.[30] The NYJ clone, typically resistant to -lactams, erythromycin, clindamycin and ciprofloxacin,[28,33] has been detected in Brazil and has completely displaced the Mexican clone in certain Mexican hospitals.[24]

In other Latin American countries, few data are available to describe the spread of individual MRSA clones fully. In a

recent study, PVL-negative ST5-SCC*mec* type IV (USA800) and ST8-SCC*mec* type IV (USA300) MRSA clones were identified in Costa Rica, and a PVL-positive ST5-SCC*mec* IV clone (USA800) was identified in Peru.[29] In Trinidad and Tobago, the Canadian MRSA clone, CMRSA-6, was observed in several major hospitals between 2000 and 2001, possibly as a result of tourism.[25]

The first CA-MRSA infections to be reported in Latin America occurred in Brazil in 2003,[34] where isolates from patients with skin and soft tissue infections (SSTIs) or septic arthritis, were found to harbor SCC*mec* type IV and PVL. In Uruguay, a large outbreak of CA-MRSA infections in jail inmates occurred,[37] in which > 1000 patients were documented with SSTIs and severe forms of pneumonia. This outbreak was caused by a CA-MRSA clone harboring SCC*mec* type IV and PVL. CA-MRSA clones belonging to CC5, CC8 and CC30 have now been identified in Brazil, Argentina, Colombia and Uruguay, and these are related to clones previously observed in the USA and Australia. In addition, community-acquired infections due to MRSA have been reported in Peru,[40] Venezuela[41] and Chile,[42,43] although some of these cases were in people returning from cities in Uruguay or Brazil where a higher incidence of community-acquired MRSA infections occurred. In a recent study in four South American countries (Colombia, Ecuador, Peru and Venezuela), Arias and colleagues found a new CA-MRSA USA300 variant in the Andean region.[36]

CLINICAL IMPLICATIONS OF MRSA CLONES

Virulence and antibiotic resistance of MRSA clones

MRSA strains cause a variety of infections, ranging in severity from cutaneous abscesses, to life-threatening necrotizing fasciitis and necrotizing pneumonia. The severity of disease is usually directly related to the production by MRSA of specific virulence factors,[44] such as toxins or protective biofilms, whereas the spread of MRSA depends partly on the ability of individual clones to acquire resistance to antibacterial agents.

Panton-Valentine Leukocidin Production

PVL, a major virulence factor for MRSA, is a secreted toxin that causes tissue necrosis and damage to immune cells. The gene encoding PVL, *pvl,* encodes two secreted subunits, designated LukS-PV and LukF-PV, which assemble together in the membranes of white blood cells, monocytes and macrophages to form pores through which cell contents leak.[45] PVL-producing MRSA strains have been associated with SSTIs and a severe form of necrotizing pneumonia.[46,47] In a US study of 422 patients with community-acquired SSTIs, 59% of isolates were identified as MRSA (mainly clone USA300), and 98% of these expressed PVL,[48] consistent with other studies.[49] The presence of PVL has now been demonstrated in both adult and pediatric MRSA infections.[49,50]

Acquisition of *pvl* by CA-MRSA clones marked a dramatic change in the epidemiology of MRSA infections, both in the community and, more recently, in hospitals.[51-53] Several studies have reported the acquisition of *pvl* by MRSA clones circulating in Latin America.[34,54,55] In Rio de Janeiro, for example, BECC isolates were shown to be positive for *pvl*, possibly following horizontal transfer from a reservoir of PVL-positive MSSA isolates.[54] In Argentina, 94% of isolates of the predominant CA-MRSA clone ST5 were found to harbor *pvl.* [35]

Biofilm production by MRSA strains

S. aureus strains routinely produce and become encased in biofilm, providing them with protection against both host defenses and antimicrobial drugs. Biofilm production is mediated by the ica operon, and this property is present in most MRSA and MSSA strains, although evidence suggests that certain MRSA clones have an enhanced ability in this regard. In 2005, the predominant variant of the BECC MRSA clone was reported to be more effective in generating biofilm and in adhering to, and invading, airway epithelial cells, than MSSA or sporadic MRSA clones.[26] In a recent Brazilian study of MRSA isolates from hospital-acquired and community-acquired MRSA infections, all 19 MRSA strains (14 Brazilian clone; 5 NYJ clone) were found to produce biofilm.[56]

Resistance in MRSA clones

MRSA, and in some countries vancomycin-resistant *enterococci*, are the most frequent antibiotic-resistant gram-positive bacteria responsible for nosocomial infections and, in the case of MRSA, community infections.[57]

HA-MRSA strains are often multidrug resistant conferred by SCC*mec* types II and III,[58]and can express resistance to fluoroquinolones, macrolides, aminoglycosides, tetracyclines and rifampin. Multidrug resistant MRSA strains can also develop reduced susceptibility or resistance to vancomycin and teicoplanin, as well as to newer antimicrobials such as quinupristin-dalfopristin, linezolid, daptomycin and tigecycline, although these occurrences are limited to a few isolated cases. *S. aureus* with reduced susceptibility to vancomycin, or vancomycin-intermediate *S. aureus* (VISA), usually develop this limited susceptibility by changing the thickness of their cell wall. Consequently, vancomycin becomes trapped in the outer wall and has reduced access to its target in the cytoplasmic membrane. *S. aureus* can also develop full resistance to vancomycin (VRSA), which is thought to be linked to the acquisition of the resistance gene *van*A from vancomycin-resistant *enterococci.*[59,60]

Clindamycin is a commonly used antibiotic for the treatment of infections caused by MSSA and MRSA, such as SSTIs. However, *S. aureus* clones have emerged with inducible resistance to clindamycin following a ribosomal target modification. Resistance to clindamycin is induced by macrolides, and can be detected following erythromycin-

mediated induction using the approximation test.[61] Studies based in the USA report the overall prevalence of inducible clindamycin resistance in *S. aureus* isolates as 52% (50% of MRSA and 60% of MSSA isolates),[62] although this may change, since clonal shift has been shown to affect inducible clindamycin resistance.[63]

In Latin America, MRSA clones are genetically diverse, but often share in common genes that encode for multidrug resistance to -lactams, erythromycin, chloramphenicol and clindamycin, and variable resistance to rifampin, fluorquinolones and TMP-SMX. Three classes of antimicrobials, including glycopeptides, oxazolidinones and the new tetracycline derivative tigecycline, are uniformly active against these clonal variants in the region. The Brazilian clone is sometimes only sensitive to vancomycin, tigecycline, linezolid and daptomycin. Although there are reports indicating heteroresistance to vancomycin in the Brazilian clone, there is currently little evidence to suggest that VISA and/or VRSA are a significant issue in Latin America. However, it will be important to monitor the situation across the region in order to identify any changes to the pattern of antimicrobial resistance as early as possible. The Cordobes/Chilean and NYJ clones, and in some places also the pediatric clone, are multidrug resistant. Usually, the Cordobes/Chilean clone is susceptible to glycopeptides, linezolid, TMP-SMX, minocycline and rifampin, while the NYJ clone is sensitive to glycopeptides, linezolid, TMP-SMX, rifampin and gentamicin. Careful use of antibiotics is an important strategy for limiting antimicrobial resistance. For example, high level resistance of the Brazilian clone to mupirocin has been reported in Brazilian hospitals,[38] but recent evidence suggests that resistance can be reduced by controlling mupirocin use.[64]

MRSA clones in hospital and community settings

Isolates from nosocomial MRSA infections, typically collected > 72 hours following hospital admission, usually, but not always, contain MRSA clones harboring SCC*mec* type I, II or III (Table 1). These clones produce bacteremia, pneumonia or urinary tract infections more frequently than they cause SSTI.[31,65] Nosocomial MRSA is usually reported as an adult pathogen, but has also been associated with infections in pediatric and neonatal intensive care units.[24,66]

Isolates from community-acquired MRSA infections, typically collected < 72 hours after admission to hospital, usually contain CA-MRSA clones that harbor SCC*mec* type IV and produce SSTI (Table 1). These clones tend to be sensitive to most antimicrobials, with the exception of erythromycin and ciprofloxacin, and commonly produce the virulence factor PVL.

RECOMBINATION BETWEEN COMMUNITY AND HOSPITAL MRSA CLONES

There is growing evidence that virulence genes can be transferred between HA- and CA-MRSA strains. For example, SCC*mec* type IV traits, usually associated with CA-MRSA, have been observed in nosocomial MRSA strains with susceptibility to four or more antimicrobials,[67] suggesting that CA-MRSA clones have been introduced into the hospital and are now circulating as nosocomial pathogens. Similarly, biofilm- and enterotoxin-producing, non-multidrug resistant MRSA that displayed PFGE patterns similar to USA800 caused severe nosocomial infections in two Brazilian hospitals in 2007.[68] Clones originating in hospitals have also been found to be spreading in the community. In Brazil, MRSA strains isolated from the nasopharyngeal passages of children recently admitted to hospital between 2000 and 2001, were found to be multidrug resistant and harboring SCC*mec* type III.[69]

INFLUENCE OF MRSA CLONES ON DISEASE AND CLINICAL PRACTICE

MRSA clones and nasal carriers

In a recent study, over 7% of hospital admissions were estimated to be nasal carriers of MRSA,[70] with the nares potentially serving as a colonizing point and reservoir for further infection. While most carriers of *S. aureus* are thought to be colonized by a single *S. aureus* clone, approximately 7% of carriers in one study were found to be 'discordant' carriers, colonized by more than one strain, and in some cases carriers were colonized by MRSA and MSSA strains simultaneously.[71] In discordant carriers, the presence of multiple strains of *S. aureus* presents the opportunity for horizontal genetic information exchange between strains.[71]

MRSA clones isolated from the anterior nares can be varied, but are often community clones.[70,72] In a homeless population study in the USA,[72] 6.2% of individuals carried nasal MRSA clones, most of which were the CA-MRSA clones USA300 and USA1000. In children within Brazilian day-care centers, several MRSA clonal types, including SCC*mec* types IIIA, IV and V, have been identified.[73]

Studies suggest that nasal carriers of *S. aureus* may develop infection at a further site with the same clone. For example, in one study, > 82% patients who developed bacteremia carried identical *S. aureus* clones in the anterior nares.[74] Furthermore, clones present in the anterior nares were shown to appear in bacteremia infections in the same patients up to 14 months later. In another study, > 67% patients with clinical MRSA infections were found to carry MRSA in the nares, and nasal carriers of MRSA carried an enhanced risk of MRSA infections at other sites compared with the remainder of the population.[75] Healthcare workers are also at risk of becoming carriers with the same clones that are present in hospitalized patients,[76] and risk transmitting this pathogen to close household contacts.[77]

MRSA clones and skin and soft tissue infections

MRSA is a prevalent and widespread cause of SSTIs. In a US study, MRSA was the most common pathogen-causing SSTI identified in emergency departments, with a prevalence of 59% overall.[48] Of the MRSA isolates, 72% were a single strain, USA300-0114, which harbored SCC*mec* type IV and was positive for PVL. These isolates were associated with superficial infections and abscesses, and with deeper infections and osteomyelitis.[48] MRSA was also the most common pathogen associated with SSTIs requiring surgical debridement in a 7-year study in Houston.[78]

While most of the MRSA strains causing SSTIs are of community origin worldwide, differences in clonality and resistance pattern of MRSA strains between close geographic areas have been reported. In California, for example, CA-MRSA accounted for 93% of SSTIs in San Francisco General Hospital between 2000 and 2002, but only for 69% in Stanford University Hospital; by 2002, PVL-positive ST8-SCC*mec* type IV (USA300) was the predominant strain in San Francisco, showing sensitivity to most antimicrobials, whereas the multidrug resistant clone ST5-SCC*mec* type II (USA100) was the predominant clone causing SSTI at Stanford University Hospital.[79] This study highlights the importance of local surveillance knowledge, even at the level of individual hospitals within the same vicinity, when choosing antimicrobial therapy for community-based SSTIs.

In Latin America, limited data are available to draw conclusions on the associations of clones with SSTIs. In the first report of community-acquired infections in the region, Ribeiro and colleagues[34] observed PVL-positive SCC*mec* type IV CA-MRSA strains in two patients with SSTI and one with septic arthritis, which corresponded to the Oceania Southwest Pacific clone (OSPC) from Australia, and shared genotypic characteristics with CA-MRSA strains in the USA and in Europe. A surveillance study conducted in 2005 in Cordoba, Argentina, found that 90% of infections caused by CA-MRSA were SSTIs, and 89% were caused by CC5:ST5 SCC*mec* type IVa-c strains,[35] whereas in Costa Rica, clones CC5:ST5 SCC*mec* type IV (USA 800) and CC8:SLV8 SCC*mec* type IV (USA 300) were found in community isolates from patients with SSTI, both of which were negative for PVL.[29]

MRSA clones and bacteremia

Data from the SENTRY Antimicrobial Surveillance Program in Argentina, Brazil, Chile, Colombia, Venezuela and Uruguay, have shown that MRSA is a common cause of nosocomial bacteremia, with a prevalence of 21.6% among bloodstream infection isolates.[80] MRSA nosocomial bacteremia causes severe complications, including infectious endocarditis,[81] and is associated with elevated morbidity and mortality.[82] The selection of antibiotic treatment and the duration of treatment for MRSA nosocomial bacteremia is one of the most controversial issues in medicine.[81,82]

Bacteremia can be caused by both CA- and HA-MRSA clones, and the severity of disease is dependent on clonal type. In a recent study,[83] SCC*mec* type II HA-MRSA clones were found to cause higher mortality than SCC*mec* type IVa CA-MRSA clones, whereas SCC*mec* type IVa clones caused greater metastatic infection. Also, while the majority of community-acquired and hospital-acquired bacteremias were caused by SCC*mec* type IVa and SCC*mec* type II MRSA clones, respectively, SCC*mec* type IVa was present in some hospital-acquired bacteremias, and SCC*mec* type II was present in some community-acquired bacteremias.[83]

MRSA clones and infectious endocarditis

MRSA is a common pathogen in infectious endocarditis (IE), with prevalence of over one third in some countries, including Brazil (37.5%) and the USA (37.2%).[81] *S. aureus* IE is usually acquired outside hospital, but predominates as a healthcare-associated infection, which accounts for 54% of cases in Brazil.[81] The first reported case of IE in Brazil caused by CA-MRSA was published in 2008,[84] and was attributed to MRSA harboring SCC*mec* type IV and positive for PVL. In Korea, a PVL-negative CA-MRSA clone ST72 SCC*mec* IVa has been identified as the cause of IE infections in previously healthy individuals with no reported risk factors for IE.[85]

CONCLUSION: CURRENT CHALLENGES AND FUTURE DIRECTIONS

Molecular epidemiological studies have highlighted the continuing global evolution and spread of MRSA clones with increased resistance to antimicrobial drugs and enhanced virulence. The factors contributing to the dissemination of MRSA clones are only partially understood, but are thought to include the migration of human populations, ineffective methods to control transmission of MRSA from infected patients, and treatment strategies, including the inappropriate use and choice of antibiotics.[86,87] In hospitals, patients already carrying MRSA when admitted are at greater risk of developing an infection derived from the colonized bacteria, or of transmitting MRSA to other patients.

In Latin America, pandemic clones are commonplace in hospitals across the region, and community-associated infections are growing in number.[1] Clones circulating in the region show genetic diversity, although common genes encoding multidrug resistance to antimicrobials are expressed. Enhanced pathogenic properties, including production of biofilms and production of enterotoxins, have been described for certain clones, and the ability of nosocomial and community clones to interchange genetic material has also been identified.

However, surveillance data for specific MRSA clones within the region is limited,[1] with existing data biased towards more developed countries and sophisticated research

centers. Paradoxically, countries showing the highest prevalence of nosocomial MRSA infections, such as Peru, often provide very little information with regard to molecular epidemiology and clinical outcome. Regional surveillance programs, using central reference laboratories and integrating information from health centers with different complexities, are required if we are to understand more fully the developing pattern of MRSA infections across Latin America, and to design better treatment and prevention strategies.

IMPLICATIONS FOR CLINICAL PRACTICE

- The characteristics of different MRSA clones are associated with clinical presentation and outcomes.
- Clonal dissemination is rapid for both CA-MRSA and HA-MRSA, and recombination between CA and HA clones is taking place.
- Regional molecular epidemiology programs are required to understand more fully the developing pattern of MRSA infections across Latin America.
- More accurate information on the precise distribution of clones in the region may help clinicians in understanding the risk of infection by certain clones and in choosing appropriate empiric antimicrobial therapy.

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