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Emerging multidrug resistance in community-associated *Staphylococcus aureus* involved in skin and soft tissue infections and nasal colonization

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Background: *Staphylococcus aureus* is a major pathogen causing significant morbidity and mortality worldwide. The emergence of MDR *S. aureus* strains in the community setting has major implications in disease management. However, data regarding the occurrence and patterns of MDR community-associated *S. aureus* sub-clones is limited.

Objectives: To use whole-genome sequences to describe the diversity and distribution of resistance mechanisms among community-associated *S. aureus* isolates.

Methods: *S. aureus* isolates from skin and soft tissue infections (SSTIs) and nasal colonization were collected from patients within 10 primary care clinics from 2007 to 2015. The Illumina Miseq platform was used to determine the genome sequences for 144 *S. aureus* isolates. Phylogenetic and bioinformatics analyses were performed using *in silico* tools. The resistome was assembled and compared with the phenotypically derived antibiogram.

Results: Approximately one-third of *S. aureus* isolates in the South Texas primary care setting were MDR. A higher proportion of SSTI isolates were MDR in comparison with nasal colonization isolates. Individuals with MDR *S. aureus* SSTIs were more likely to be African American and obese. Furthermore, *S. aureus* populations are able to acquire and lose antimicrobial resistance genes. USA300 strains were differentiated by a stable chromosomal mutation in *gyrA* conferring quinolone resistance. The resistomes were highly predictive of antimicrobial resistance phenotypes.

Conclusions: These findings highlight the high prevalence and epidemiological factors associated with MDR *S. aureus* strains in the community setting and demonstrate the utility of next-generation sequencing to potentially quicken antimicrobial resistance detection and surveillance for targeted interventions.

Introduction

Since the discovery of *Staphylococcus aureus*, a major challenge has been its remarkable ability to acquire resistance to antibiotics. The emergence of community-associated MRSA (CA-MRSA) has resulted in an epidemic of skin and soft tissue infections (SSTIs) in the USA.[1,2] Whereas MDR has been well described among hospital-associated *S. aureus* clones, community-associated *S. aureus* clones have retained susceptibility to non-β-lactam antimicrobials, including macrolides, tetracyclines, fluoroquinolones, lincosamides and trimethoprim/sulfamethoxazole. However, the increased use of these antimicrobials could drive the emergence of new MDR sub-clones of community-associated *S. aureus*, complicating disease management. The emergence of resistance to these agents among USA300 strains poses a tremendous challenge for treating both community- and healthcare-associated *S. aureus* infections.[3–6]

With rapidly advancing technology, microbial WGS is positioned to soon become a viable option in the routine clinical laboratory.[7–9] WGS provides valuable information in reconstructing the evolution

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of antimicrobial resistance and has the potential to substantially increase the speed of antimicrobial resistance detection in the practice setting.[10–13] With the ever-increasing rise of bacterial drug resistance, the need for rapid and reliable methods to detect its emergence and predict antimicrobial susceptibility has never been more imperative.

This study aimed to: (i) describe the population structure, diversity and distribution of resistance mechanisms among community-associated *S. aureus* isolates; and (ii) determine the extent to which the genotype is predictive of resistance.

Materials and methods

Study setting and population

We performed this investigation using clinical and isolate information from a well-described cohort of patients with *S. aureus* SSTIs or nasal colonization in the South Texas primary care setting. Details of this cohort have been described previously.[14,15] Briefly, this study was conducted in collaboration with ten primary care clinics within the South Texas Ambulatory Research Network, a practice-based research network composed of urban, suburban and rural primary care clinics distributed throughout the South Texas region, from 2007 to 2015. Patients were eligible for study enrolment if they provided informed consent, were 18 years of age or older, and presented to one of the participating clinics with a purulent SSTI. Patients were excluded if they were pregnant, incarcerated or had impaired decision-making capacity. Nasal isolates were from patients who presented to these clinics from February to May 2015 to assess for *S. aureus* nasal colonization. The subsequent analyses conducted in this study were limited to isolates confirmed to be *S. aureus* and the patients from whom they were obtained.

Ethics

The institutional review board at the UT Health Science Center San Antonio approved the study.

Microbiological analysis

Samples were plated onto blood agar plates and incubated at 35°C for 24 h, then sub-cultured to MRSA-selective agar (MRSASelect chromogenic agar plates; Bio-Rad Laboratories). Latex agglutination tests (StaphAurex®; Thermo Fisher Scientific) and phenotypic screening tests (cefoxitin) were used for the identification and isolation of MRSA. Vitek 2 AST-GP75 cards (bioMérieux) were used to determine the susceptibility of *S. aureus* study isolates to 14 antibiotics. D-zone tests were performed to identify inducible clindamycin resistance. Mupirocin susceptibility testing was conducted using gradient diffusion testing (Etest, bioMérieux). Antimicrobial MICs were interpreted according to the CLSI document M100-S14 (2014).[16] Standard definitions of MDR were used.[17]

DNA sequencing and analyses

DNA extraction was conducted on the MagNA Pure 96 Instrument for automated DNA extraction (Roche Life Science, Indianapolis, IN, USA). Sequencing libraries were prepared using the NexteraXT DNA sample preparation kit (Illumina Inc.) following the manufacturer's instructions and sequenced on a MiSeq sequencing instrument (Illumina Inc.).

Sequencing data were imported and analysed using CLC Genomics Workbench 8.1 (Qiagen, Redwood City, CA, USA). Paired-end reads were mapped to reference strain FPR3757 (accession number NC_007793).[18] The Fixed Ploidy Variant Detection tool was used to identify SNPs and the Indels and Structural Variants tool was used to identify insertions and deletions.[19] SNPs were included in analyses if that position contained at least 15 high-quality reads and ≥90% of them supported an alternative allele different from the FPR3757 reference. An *in silico* SNP validation was performed to assess SNP frequency with varying coverage levels (Table S1, available as Supplementary data at *JAC* Online). Strain whole-genome sequence FASTQ files have been deposited with NCBI under BioProject PRJNA352260.

For comparative genome evaluation, SNPs were used as a measure of genetic pairwise distances between strains. An SNP matrix was generated using the Reference Sequence Alignment-based Phylogeny builder (REALPHY: http://realphy.unibas.ch/fcgi/realphy). The SNP matrix was uploaded onto MEGA7 and CLCGenomics Workbench 8.5.1 for phylogenetic analyses. Phylogeny was inferred using neighbour joining and the maximum likelihood method based on the Jukes–Cantor model with 500 bootstrap replicates. Consistent with previous literature, clusters of strains were indicated by bootstrap values of >70% for maximum likelihood and neighbour-joining analyses.[4]

MLST was determined from the sequence data by extracting the sequence at the specific loci of the seven housekeeping genes using the CLCGenomics Workbench 8.5.1 and the *S. aureus* MLST scheme (www.pubmlst.org; downloaded November 2015). Isolates were considered to be USA300 if they were ST8 and had the Panton–Valentine leucocidin (PVL) genes, as previously validated.[20,21]

Mobile genetic elements (MGEs) were detected *in silico*. Sequence reads were assembled *de novo* into contigs and were used to determine the presence and absence of MGEs. The assembled contigs were screened with PlasmidFinder to identify circular and integrated plasmids using a subset of replicon sequences from 139 fully sequenced plasmids associated with *S. aureus*.[22]

Resistome

To assemble the resistome, the presence and absence of known antimicrobial resistance genes was identified using the ARG-ANNOT (Antibiotic Resistance Gene-ANNOTation) database followed by manual searching for chromosomal genes with amino acid variants.[23] The genetic elements and accession numbers associated with susceptibility among the *S. aureus* isolates are listed in Tables S2 and S3.

Discrepancy investigation

Discrepancies were defined as discordances between susceptibility results using Vitek 2 and predicted genotypic susceptibility. Discrepancies were investigated using gradient diffusion testing (Etest, bioMérieux). Concordance was defined as agreement between susceptibility results from Vitek 2 or gradient diffusion with genotype. Major errors (MEs) occur when the phenotypic result (Vitek 2) is susceptible and the genotypic prediction is resistant. Very major errors (VMEs) occur when the phenotypic result (Vitek 2) is resistant but the genotypic prediction is susceptible. The initial phenotypic and genotypic analysis of resistance was conducted blind by two investigators.

Statistical analyses

Statistical analyses were performed using SPSS 23.0® (IBM Corp, Armonk, NY, USA). The χ^2 test or Fisher's exact test was used for dichotomous or categorical variables. Student's *t*-test was used for continuous variables. $P < 0.05$ indicated statistical significance.

Results

MLST of S. aureus

We sequenced 144 *S. aureus* isolates (112 from SSTIs and 32 from nasal colonization) recovered from 144 patients. Seventy-one strains were MRSA and 73 were MSSA. All MRSA isolates belonged

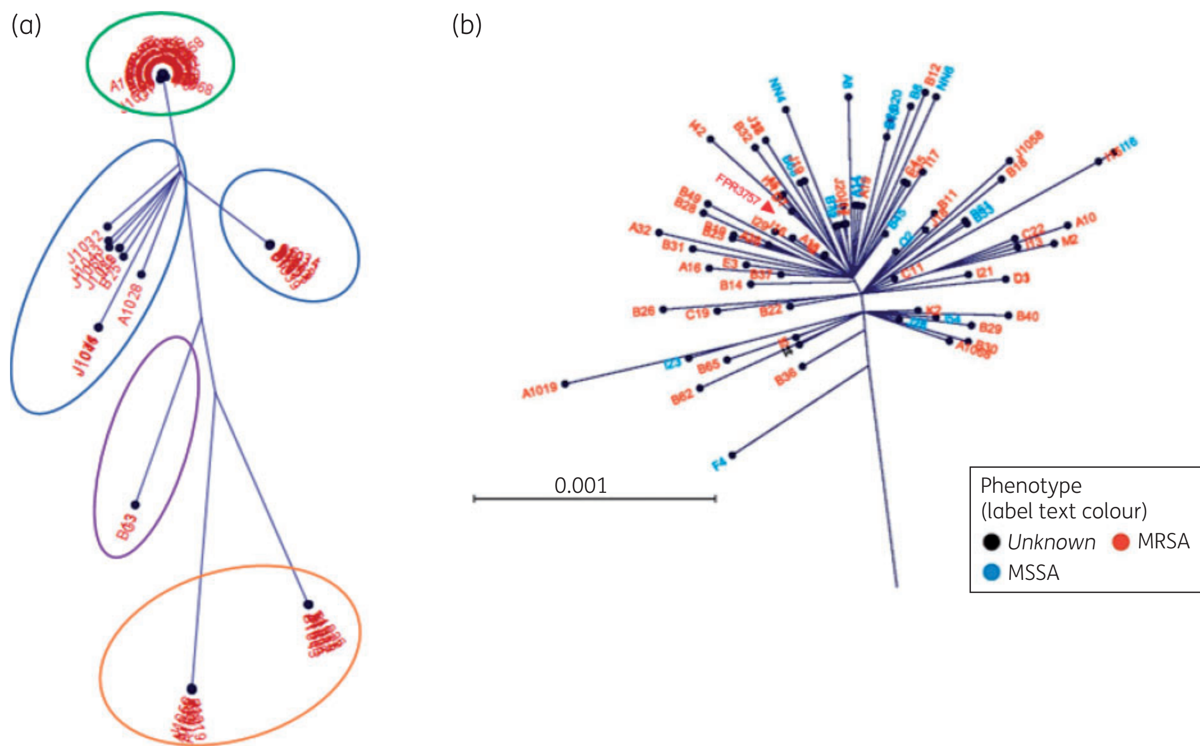

Figure 1. SNP-based phylogenetic analyses of *S. aureus* strains. (a) Radial phylogenetic tree mapping the isolates based on the concatenated SNP distances. Group 1 (green ring) comprised primarily ST8 clustered tightly with reference FPR3757. Group 2 (blue rings) comprised two groups similarly distant from FPR3757. Group 3 (purple ring) comprised three ST59 isolates. Group 4 (orange ring) comprised ST30 and ST45 isolates. (b) Zoomed-in view of Group 1 cluster composed of ST8 isolates.

to the ST8 clonal group (Figure S1). Although, the majority of MSSA belonged to ST8 and ST5, we identified a variety of unique isolates that belonged to other ST types; these included livestock-associated ST97 and ST59 clones, and multiple novel MLST clonal types with single-locus variants of ST8, ST5 and ST12 (Table S4).

To estimate the population structure, sample reads were mapped onto a single core reference genome, FPR3757. One hundred and twenty-three isolates had sufficient coverage for the analyses. We identified a total of 53840 SNP sites compared with the reference sequence FPR3757. After excluding MGEs, the strains differed by an average of 3548 SNPs (range 15–47574). Based on the neighbour-joining method, the isolates fell into four clades (Figure 1). The first group comprised only ST8 isolates that grouped very tightly with FPR3757, differing by an average of 160 SNPs (range 15–1215). This magnitude of inter-strain distance is similar to previous reports.[24] Approximately 70% of the *S. aureus* isolates included in this study clustered in Group 1. Of note, methicillin-susceptible and -resistant strains were intermingled, suggesting a common lineage. Group 2 encompassed two branches that were both similarly distant from the reference strain: one group was composed mainly of ST5 strains, which are known to be predominantly hospital-acquired (HA)-MRSA strains; the other group was more heterogeneous. The third group comprised ST59 MSSA strains. The fourth group was composed mainly of ST45 and ST30 MSSA strains.

To evaluate the concordance of traditional MLST typing and WGS data, the MLST strain types were mapped onto the WGS phylogenetic tree (Figure 2). In this collection, isolates with the same MLST type predictably clustered into the same branch. Although isolates sharing the same ST clustered together, the high resolution of WGS demonstrated that the distance between individual isolates within each cluster varied substantially (Figure S2). This may suggest that the close clusters represent successful lineages that have undergone recent clonal expansion, whereas the distantly related clades may represent rarer, less successful lineages.

To identify whether particular strains clustered together by geographic region, the location of the practice site was mapped onto the WGS phylogenetic tree. The MLST and phylogenetic analysis revealed that specific clones were not necessarily specific to particular geographic locations (Figure S3), with the exception that both *S. aureus* strains from Bulverde, TX, clustered closely together. These two strains from unrelated patients were identified to be most closely related to an *S. aureus* strain (RF-122) associated with severe bovine mastitis (Figure S4).[25]

Antimicrobial resistance determinants among community-associated S. aureus

The antibiograms of 143 isolates (32 nasal isolates and 111 SSTI isolates) were analysed. Genetic determinants were specifically isolated within specific clades on the phylogenetic tree (Figure S5). Notably, the presence of resistance determinants for aminoglycosides, tetracycline, mupirocin and trimethoprim occurred primarily among ST8 isolates.

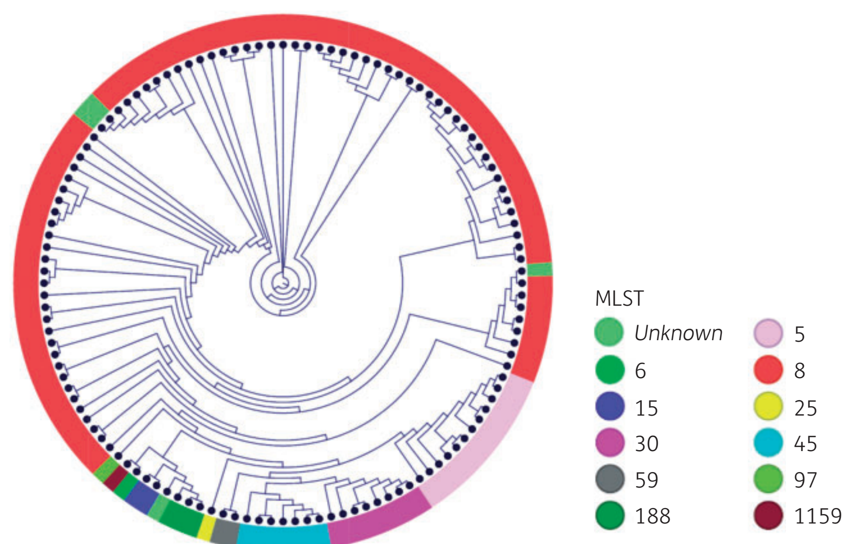

Figure 2. SNP-based phylogenetic analysis and MLST. Multilocus strain types were computationally mapped onto the phylogenetic tree. The coloured outer ring denotes the MLST type.

Table 1. Comparison of whole-genome detection of antimicrobial resistance determinants and phenotype

Antibiotic	Phenotype: susceptible #S	Phenotype: susceptible genotype S	Phenotype: susceptible genotype R	Phenotype: resistant #R	Phenotype: resistant genotype S	Phenotype: resistant genotype R	Error rate (%) VMEs	Error rate (%) MEs	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Ciprofloxacin	87	78	7	56	3	53	2.1	4.9	95	90	85	96
Clindamycin	133	133	0	10	0	10	0	0	100	100	100	100
Erythromycin	70	62	8	73	3	70	2.1	5.6	96	88	90	94
Gentamicin	141	141	0	2	0	2	0	0	100	100	100	100
Mupirocin	140	140	0	3	1	2	0.7	0	67	100	100	99
Oxacillin	71	67	4	72	2	70	1.4	2.8	97	93	93	97
Rifampicin	143	143	0	0	0	0	0	0	n/a	100	n/a	100
Tetracycline	141	141	0	2	0	2	0	0	100	100	100	100
Trimethoprim	139	139	0	4	1	3	0.7	0	75	100	100	99
Vancomycin	143	143	0	0	0	0	0	0	n/a	100	NA	100

S, susceptible; R, resistant; #S, number of isolates susceptible; #R, number of isolates resistant; PPV, positive predictive value; NPV, negative predictive value.

The predictive patterns of antimicrobial resistance determinants based on genetic mechanisms are detailed in Table 1. After discrepancy testing, the overall VMEs and MEs were 0% and 1.4%, respectively (Table S5). Upon subsequent discrepancy testing, all 9 VMEs were rectified and aligned with the genotype (Table 2). Furthermore, most MEs were also resolved after repeat phenotypic testing. The remaining MEs were from the detection of oxacillin resistance. The *mecA* gene was detected while phenotypically displaying susceptibility to oxacillin.

Epidemiological features of MDR

Approximately 31% of the isolates were MDR. Most MDR isolates were ST8 (91%); one isolate was an ST30, one isolate was ST121 and two had novel ST designations. Approximately 42% of ST8 strains were MDR. A higher proportion of SSTI isolates compared with colonizing isolates were MDR (37% versus 11%; $P<0.05$). Among SSTIs, features associated with MDR isolates included African American race ($P<0.01$) and obesity ($P=0.04$) (Table 3). Notably, there were no differences in reported prior antibiotic exposures between cases with MDR isolates compared with non-MDR isolates (17% versus 14%; $P=0.60$).

When evaluating geographic clustering, we found more than half of the MDR isolates clustered within the Inner West Side of San Antonio, a predominantly Hispanic and African American community with household incomes significantly below the state average (Figure S6a). However, the proportion of MDR strains (among areas with two or more isolates) was disproportionately higher (50% of

Table 2. Discrepancy testing of whole-genome detection of antimicrobial resistance determinants and phenotype

Error type/ antimicrobial	Isolate	Initial phenotype	Repeat phenotype [MIC, mg/L (interpretation)]	Genotype	Resolved
VMEs					
ciprofloxacin	I5	R	0.125 S	no *gyrA or grlA* mutation detected	yes
	I23	R	0.94 S	no *gyrA or grlA* mutation detected	yes
	I39	R	0.125 S	no *gyrA or grlA* mutation detected	yes
erythromycin	B23	R	0.125 S	no *erm* or *msrA* gene detected	yes
	I7	R	0.125 S	no *erm* or *msrA* gene detected	yes
	I17	R	0.125 S	no *erm* or *msrA* gene detected	yes
oxacillin	B23	OXA MIC >4 (R) FOX+	0.5 S	no *mecA* gene detected	yes
	I7	OXA MIC >4 (R) FOX+	0.25 S	no *mecA* gene detected	yes
trimethoprim	B23	R	0.04 S	no *dfrA*, *dfrG* or *dfrB* mutation detected	yes
MEs					
ciprofloxacin	A8	S	≥32 R	*gyrA* mutation detected	yes
	I7	S	8 R	*gyrA* mutation detected	yes
	I17	S	6 R	*gyrA* mutation detected	yes
	I42	S	16 R	*gyrA* mutation detected	yes
erythromycin	B30	S	32 R	*msr* gene detected	yes
	C11	S	32 R	*msr* gene detected	yes
	I5	S	48 R	*msr* gene detected	yes
	I11	S	24 R	*msr* gene detected	yes
	I21	S	64 R	*msr* gene detected	yes
	I23	S	64 R	*msr* gene detected	yes
	I24	S	48 R	*msr* gene detected	yes
	J17	S	32 R	*msr* gene detected	yes
oxacillin	A8	OXA MIC <0.25 (S) FOX−	64 R sub-colonies	*mecA* gene detected	yes
	C11	OXA MIC = 1 (S) FOX+	1 S	*mecA* gene detected	no
	I5	OXA MIC <0.25 (S) FOX−	1 S	*mecA* gene detected	no
	I11	OXA MIC = 0.5 (S) FOX−	32 R sub-colonies	*mecA* gene detected	yes

FOX+/FOX−, positive or negative, respectively, on a cefoxitin screen; OXA, oxacillin.

Table 3. Characteristics of patients with MDR compared with non-MDR community-associated *S. aureus* SSTI strains

Characteristic	MDR (*n* = 38)	No MDR (*n* = 73)	*P* value
Mean age, years (±SD)	43±12	41±13	0.56
Gender, *n* (%)			
male	20 (53)	36 (49)	0.67
Race/ethnicity, *n* (%)			
African American	6 (16)	2 (3)	0.01*
Hispanic	29 (76)	52 (72)	0.64
Diabetes, *n* (%)	11 (30)	18 (25)	0.63
Obese (BMI ≥30), *n* (%)	21 (55)	29 (40)	0.04*
MRSA phenotype, *n* (%)	31 (81)	36 (49)	<0.01*
Prior SSTI in last 90 days, *n* (%)	7 (18)	9 (12)	0.41
Prior antibiotic in last 90 days, *n* (%)	5 (13)	10 (14)	0.61

There were no cases of patients with the peripheral vascular disease, HIV infection, cancer or receipt of chemotherapy.
*Statistical significance.

isolates in this geographic region were MDR) in the north-west side of San Antonio, the location of the South Texas Medical Center (Figure S6b).

Plasmid characterization

On average, the isolates carried approximately three plasmids (range 0–6). The occurrence of pUSA300-like plasmids (e.g. pUSA02 and pUSA03) was rare and was only detected in two ST8 isolates. However, the distribution of plasmids was widespread. In the case of pSJH101 (*rep*16), its *rep* genes were detected in strains belonging to several different lineages (ST8, ST5, ST59, ST45 and ST30). This supports the notion of the potential transfer of MGEs and resistance genes among different *S. aureus* clonal lineages (Table S6).

Fluoroquinolone resistance among USA300

To explore the association of the role of antimicrobial resistance determinants in the evolution of *S. aureus*, the presence and absence of specific resistance mechanisms was mapped onto the

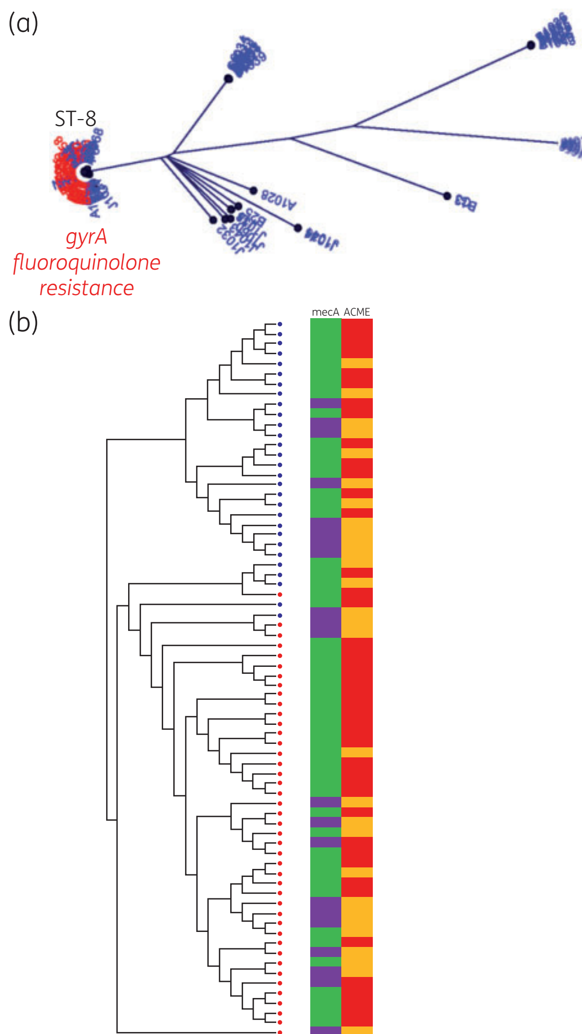

Figure 3. Fluoroquinolone resistance among *S. aureus*. (a) Radial tree of all isolates evaluated for the chromosomal mutation in *gyrA* conferring fluoroquinolone resistance (presence of chromosomal mutation is marked in red). (b) Maximum likelihood tree of USA300 *S. aureus* strains. Red indicates the presence and blue indicates the absence of chromosomal mutation in a strain. Adjacent to the tree is a panel showing the presence (green) and absence (purple) of the *mecA* gene and the presence (red) and absence (orange) of the arginine catabolic mobile element (ACME).

WGS phylogenetic tree. The phylogeny of *S. aureus* strains revealed that strains containing the mutation that confers fluoroquinolone resistance within the *gyrA* (Leu84Ser) gene clustered among USA300 strains in the ST8 cluster (Figure 3a). When evaluating the population structure of USA300 strains, the strains broadly clustered within two major clades based on the presence of fluoroquinolone resistance (Figure 3b). Furthermore, three closely related MSSA USA300 strains were found to contain the arginine catabolic mobile element (ACME), suggesting some potential instability or transfer of the SCC*mec*. These findings indicate the mosaicism of composite islands in *S. aureus*, and reveal concerns for potential under-reporting of MRSA using genotypic methods.

Discussion

The emergence of MDR *S. aureus* strains in outpatients complicates disease management and contributes to the development of persistent or recurrent community-associated MRSA infections. This study detected a high level of MDR among community-associated *S. aureus* strains in South Texas. Approximately 42% of USA300 *S. aureus* isolates were MDR. This is a sharp increase in comparison with a 2004 investigation of USA300 strains from 11 US cities, where only two MDR isolates were identfied.[26] However, there have been sporadic reports of MDR in specific patient groups. This includes reports of USA300 MDR rates as high as 46% in MSM in San Francisco and Boston. In Taiwan, 61% of CA-MRSA (ST59) strains were resistant to four or more non-β-lactam agents among paediatric patients.[3,27] To our knowledge, the present study is the first to describe high-level *S. aureus* MDR in Texas.

Resistance determinants were distributed among different clades and strain types. This suggests that the loss and acquisition of resistance genes varied not only between but also within the clades. Almost all MDR *S. aureus* were found in the ST8 and ST30 clades. Furthermore, while we found a higher proportion of MDR *S. aureus* among SSTI compared with carrier strains, the proportion of colonizing strains containing three or more resistance mechanisms was >10%. This further supports the notion that the nares are an important reservoir and site for transmission of antimicrobial resistance determinants.

This study identified a cluster of three isolates resistant to trimethoprim/sulfamethoxazole. Two of the trimethoprim-resistant isolates harboured *dfrG*, one of which also harboured *dfrK*. Previously, both *dfrG* and *dfrK* were found to play a role in trimethoprim resistance in *S. aureus* of animal origin. However, recent work evaluating trimethoprim resistance among *S. aureus* strains from Europe, Asia and Africa found *dfrG* to be the predominant genetic determinant.[28,29] To the best of our knowledge, this is the first report of *dfrG* and *dfrK* in *S. aureus* from a human infection in this region. Consistent with prior studies, we found co-resistance to trimethoprim and tetracycline (*tetK*), suggesting there may be a similar link between these two resistance genes.[29,30] These findings have major implications for outpatient treatment. In a prior study describing outpatient treatment patterns of purulent SSTIs, trimethoprim/sulfamethoxazole was the most commonly prescribed antibiotic, followed by doxycycline and clindamycin.[31]

This investigation identified African American race and obese individuals with a higher proportion of MDR *S. aureus*. While studies have reported African American race as a risk factor for MRSA infections,[26,32,33] this is the first study to observe that this population may also be at increased risk of acquiring MDR *S. aureus* strains. Furthermore, the majority of MDR strains clustered in an area of lower socio-economic status composed predominantly of African Americans and Hispanics. It can be speculated that geographic areas with different socio-economic settings and networks, and uneven distribution of MRSA can contribute to the observed disparity; further investigations are required.[33]

The density of MDR *S. aureus* was geographically highest in the north-west side of San Antonio, the location of the South Texas Medical Center. Consistent with other studies, this indicates the possibility of direct acquisition of resistance determinants from MDR HA-MRSA strains.[34,35] Further studies are needed to determine the

role hospitals play, including antibiotic selection pressures, in the spread of MDR *S. aureus* strains back into the community.

The phylogeny of *S. aureus* strains revealed that strains containing the mutation that confers fluoroquinolone resistance within *gyrA* (Leu84Ser) clustered only among USA300 strains. When evaluating the population structure of USA300 strains, we identified the strains as clustered within two major clades based on the presence of fluoroquinolone resistance. This is consistent with prior studies suggesting that the use of fluoroquinolones might have further promoted the clonal expansion of USA300, and that dominant *S. aureus* strains might have been selected because of resistance to fluoroquinolones and not just methicillin.[4,36] Fluoroquinolone resistance has been previously described as a marker of successful healthcare-associated MRSA clones, which may be what is driving the selection of fluoroquinolone resistance and MDR among isolates found in close proximity to the medical centre observed in this study.[36]

This study described the predictive patterns of antimicrobial resistance determinants based on genetic mechanisms most commonly observed among community-associated *S. aureus* isolates. The final results demonstrated a high level of concordance, comparable with the error rates for current phenotypic methodologies, including the Vitek 2 and the Phoenix automated microbiology systems.[37]

Interestingly, almost all errors were rectified with subsequent discrepancy testing that aligned to the genotype. The remaining errors were due to the genotypic detection of the *mecA* gene while phenotypically displaying susceptibility to oxacillin. Phenotypically oxacillin-susceptible and *mecA*-positive *S. aureus* strains have been increasingly reported; however, their clinical significance is unknown.[38,39] These discrepancies underscore the impact of potential laboratory errors, mixed infections or within-host variation of populations on observed phenotypic variation. Stanczak-Mrozek *et al.*[40] identified a range from one to eight *S. aureus* sub-isolates with genetic and antimicrobial resistance variation per patient.

This study has limitations. Firstly, the geographic associations were limited to the locations of the clinics that served the patients and not specific household addresses. The sequences were mapped onto a reference genome, FPR3757; therefore, DNA not found in the reference strain was not evaluated. This study is subject to sampling bias from the participating clinics. Lastly, other important epidemiological factors that may be associated with *S. aureus* transmission (e.g. previous healthcare exposures, contacts, social networks) were not analysed.

In summary, this study found that MDR of community-associated *S. aureus* strains has emerged and is an important cause of SSTIs in Texas. This underscores the need to develop outpatient surveillance strategies and technologies to detect antimicrobial resistance rapidly.

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Transparency declarations

None to declare.

Supplementary data

Tables S1 to S6 and Figures S1 to S6 appear as Supplementary data at *JAC* Online.

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