ORIGINAL ARTICLE

First report of methicillin-resistant *Staphylococcus aureus* carrying the *mecC* gene in human samples from Iran: prevalence and molecular characteristics

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Abstract

There is a lack of information concerning *mecC* clinical methicillin-resistant *Staphylococcus aureus* (MRSA) strains throughout the world. In the present survey, 345 MRSA strains were characterized by antimicrobial susceptibility testing and staphylococcal cassette chromosome *mec* element (SCC*mec*) typing. *mecC*-positive MRSA isolates were characterized by study of biofilm formability, adhesion and virulence analysis, multilocus sequence typing, accessory gene regulator (*agr*) typing, S. aureus protein A locus (*spa*) typing and staphylocoagulase typing. The present study found ten SCC*mec* types, with the majority being SCC*mec* type III (38.3%). The presence of *mecC* was confirmed in three isolates from skin wounds (two isolates) and burn wounds (one isolate). All the *mecC*-positive isolates carried SCC*mec* XI and belonged to *coa* type III. Molecular typing showed that these isolates belonged to clonal complex/ST130-*spa* type t843-*agr* type III (two isolates) and clonal complex/ST599-*spa* type 5930-*agr* type I. The presence of SCC*mec* type IV confirms the hypothesis of extensive infiltration from the community to the hospital. Detection of MRSA isolates harbouring the *mecC* gene highlights the need to perform routine detection methods and molecular investigations in order to identify these emerging strains and limit their transfer in hospitals and communities.
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Keywords: *Agr* allotype, *mecC*, MLST, MRSA, PCR, *spa*, *Staphylococcus aureus*
Original Submission: 3 September 2020; **Revised Submission:** 30 November 2020; **Accepted:** 1 December 2020
Article published online: 5 December 2020

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Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) is an opportunistic pathogen responsible for many nosocomial infections [1]. Over the past few decades, the emergence of MRSA strains in the community and infection in patients without previous healthcare contact has become a matter of concern worldwide [1,2]. Resistance to methicillin is mediated by the *mecA* gene, which encodes an altered penicillin-binding protein (PBP2a/PBP2′) and is carried on the staphylococcal cassette chromosome *mec* element (SCC*mec*) [3]. SCC*mec* is composed of two essential genetic components (the *ccr* gene complex (*ccr*) and the *mec* gene complex) and the junkyard (J) regions. The *ccr* gene complex consists of *ccr* genes and surrounding open reading frames, which mediate the mobility of SCC*mec*. The *mec* gene complex is composed of the *mecA* gene, regulatory genes of *mecR1-mecI* and different insertion sequences. Several types of SCC*mec* elements have been described on the basis the combinations of *mec* and *ccr* complexes. Recently, *mecC*, a *mecA* homolog provisionally named $mecA_{LGA251}$, was reported in a small number of animal sources [4]. The *mecC* is located in a new SCC*mec* cassette type XI and exhibits 69% homology with *mecA* and 63% identity to the PBP2a encoded by *mecA* [5].

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https://doi.org/10.1016/j.nmni.2020.100832

Limited data are available on MRSA isolates carrying the *mecC* gene in Iran. Hence, the present research investigated the distribution of different SCC*mec* types and the prevalence of *mecC*-positive MRSA isolates. Multilocus sequence typing (MLST), accessory gene regulator (*agr*) typing, S. aureus protein A locus (*spa*) typing and staphylocoagulase typing were used to characterize the genotype of the *mecC*-positive MRSA isolates.

Materials and methods

Bacterial isolates

In the present study, 345 MRSA strains were randomly selected from stored isolates collected from different clinical microbiology laboratories between 2015 and 2019 in Tehran, Iran. The sources for the isolation of the strains included skin wounds (27.8%), purulent exudates (18.8%), burn wounds (13.4%), urine (11.3%), blood (10.4%), surgical wounds (10.1%), respiratory tract secretions (5.8%) and other body fluids (1.5%). Ethical approval for this study was obtained from the ethics committee of Shahid Beheshti University of Medical Sciences in Tehran, Iran (IR.SBMU.MSP.REC.1398.816). All strains were isolated and identified using standard bacteriologic techniques and PCR analysis of *fem* and *nuc* genes [6]. MRSA strains were identified by the disc diffusion method using cefoxitin (30 µg) discs on Müller-Hinton agar (Merck, Germany) using the 2019 Clinical and Laboratory Standards Institute (CLSI) guidelines and detection of the *mecA* gene as previously described [6].

Evaluation of antimicrobial activities

Antibiotic susceptibility was performed by the Kirby-Bauer disc diffusion method against kanamycin (KAN), gentamicin (GEN), tobramycin (TOB), amikacin (AMK), clindamycin (CLI), quinupristin/dalfopristin (SYN), tetracycline (TET), erythromycin (ERY), rifampin (RIF), teicoplanin (TEC), linezolid (LIN), ciprofloxacin (CIP) and trimethoprim/sulfamethoxazole (SXT) (Mast, UK) and interpreted according to the 2019 CLSI guidelines. MIC values for the antibiotics vancomycin and mupirocin were determined using the broth microdilution method. Test performance was monitored using *S. aureus* ATCC 25923, ATCC 43300 and ATCC 29213 strains.

mecC gene detection

All MRSA isolates were subjected to PCR assay for the presence of the *mecC* gene with forward (5′-GAA AAA AAG GCT TAG AAC GCCTC-3′) and reverse (5′-GAA GAT CTT TTC CGT TTT CAG C-3′) primers as previously described by García-Álvarez *et al.* [7]. Positive PCR products were sequenced to confirm the identification of the *mecC* gene. MRSA isolates harbouring *mecC* were subjected to PCR targeting *S. aureus mec* complex E and *ccr* complex 8 to confirm the presence of SCC*mec* type XI [8].

Phenotypic analysis of biofilm formation

The MRSA isolates carrying the *mecC* gene were investigated for biofilm formation using *in vitro* microtitre plate assay according to the procedure described by Yousefi *et al.* [9]. The *Staphylococcus epidermidis* ATCC 35984 strain was used as the control positive strain for biofilm formation.

DNA isolation and screening for resistance, virulence and biofilm-related genes

Genomic DNA extraction was carried out using the phenol–chloroform method as described previously [10]. All isolates were screened for resistance encoding genes, namely: *vanA, vanB, mupB, mupA, fusA, fusB, fusC, msr(A), msr(B), erm*(A), *erm*(B), *erm*(C), *tetM*, *tetL*, *tetO*, *tetK*, *ant* (4′)-*Ia, aac* (6′)-*Ie/aph* (2″) and *aph* (3′)-*IIIa* and virulence encoding genes including exfoliative toxin genes (*eta* and *etb*), Panton-Valentine leukotoxin (*pvl*) and toxic shock toxin (*tst*) genes by PCR assay with oligonucleotide primers as previously described. PCR assay was also used to evaluate biofilm by the presence of *icaABCD, can, ebp, fnbB, fnbA* and *bap* genes [10].

Molecular typing methods

The MRSA isolates were subjected to multiplex PCR to type and subtype the SCC*mec* elements using the specific primers and protocol described by Ghaznavi-Rad *et al.* [11]. The MRSA isolates carrying the *mecC* gene underwent *spa* typing by amplification of the polymorphic X region of the *spa* gene by PCR with forward (5′-AGACGATCCTTCGGTGAGC-3′) and reverse (5′-GCTTTTGCAATGTCATTTACTG-3′) primers as recommended by Harmsen *et al.* [12]. The *agr* types of *mecC*-positive isolates were determined by multiplex PCR assay as described by Gilot *et al.* [13]. Coagulase typing was also performed by multiplex PCR assay according to the procedure of Hirose *et al.* [14]. The *mecC* positive isolates were further characterized by MLST by amplifying and sequencing seven housekeeping genes (*pta, arcC, tpi, aroE, gmk, yqiL, glp*). Sequence types (STs) were determined by submitting the allelic profile to the online MLST database website (https://pubmlst.org/).

Results

The current analysis documented resistance in 77.4% of isolates for GEN, followed by 76.5% for ERY, 71.9% for TET, 58.3% for AMK, 52.2% for CIP, 50.7% for KAN, 46.1% for CLI, 29.9% for TOB, 16.2% for RIF, 14.5% for SXT, 11.6% for SYN and 11.3% for MUP. In total, 15 resistance patterns were identified, wherein

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GEN, AMK, ERY (17.7%, 61/345), GEN, KAN, AMK, TET, TOB, ERY, CLI, CIP (10.1%, 35/345) and GEN, KAN, AMK, TET, ERY, CLI, CIP, SXT (8.1%, 28/345) were the top three frequently identified patterns. All the isolates were susceptible to linezolid and vancomycin. Table 1 displays the resistance pattern and distribution of samples in MRSA strains isolated from clinical sources. Isolates were distinguished into ten SCC*mec* types. The predominant SCC*mec* type was III, which included 132 isolates (38.3%), followed by type IVa (21.4%), type II (10.1%), type V (8.4%), type I (7.5%), type IVb (7.5%), type IVc (3.5%), type IVh (1.5%), type IVd (0.9%) and type XI (0.9%). Fig. 1 shows the analysis of SCC*mec* types based on sources of isolates.

The overall prevalence of mupirocin resistant MRSA strains was found to be 11.3%, of which 20 isolates (5.8%) had low-level mupirocin resistance and 19 (5.5%) had high-level mupirocin resistance. All MRSA strains with high-level mupirocin resistance carried the *mupA* gene and belonged to SCC*mec* types III (52.6%), II (36.9%) and I (10.5%). Fig. 2 provides summary data on the distribution resistance profiles among different SCC*mec* types. Analysis revealed that three isolates

TABLE 1. Resistance pattern and distribution of samples in 345 methicillin-resistant *Staphylococcus aureus* strains related to clinical infections

No. of antibiotic classes	Antibiotic resistance pattern	Isolates, *n* (%)	Sample source (*n*, %)
9	GEN, KAN, AMK, TET, TOB, ERY, CLI, CIP, SXT	21 (6.1)	SW (3, 14.3), BW (6, 28.5), SuW (3, 14.3), U (9, 42.9)
	GEN, KAN, AMK, TET, ERY, CLI, CIP, RIF, SYN	19 (5.5)	SW (6, 31.6), B (10, 52.6), U (3, 15.8)
	GEN, KAN, AMK, TET, TOB, ERY, CLI, CIP, MUP	15 (4.3)	SW (10, 66.7), BW (3, 20), P (2, 13.3)
8	GEN, KAN, AMK, TET, ERY, CLI, CIP, SXT	28 (8.1)	SW (4, 14.3), BW (6, 21.5), SuW (5, 17.8), B (5, 17.8), P (8, 28.6)
	GEN, KAN, TET, TOB, ERY, CIP, RIF, SYN	15 (4.3)	SW (3, 20), B (5, 33.3), BF (1, 6.7), U (6, 40)
	GEN, AMK, TET, TOB, ERY, CLI, CIP, MUP	17 (4.9)	SW (5, 29.4), BW (9, 52.9), SuW (3, 17.7)
	GEN, KAN, AMK, TET, TOB, ERY, CLI, CIP	35 (10.2)	SW (7, 20), SuW (10, 28.6), B (6, 17.1), P (12, 34.3)
7	GEN, KAN, TET, ERY, CLI, CIP, RIF	20 (5.8)	BW (8, 40), P (4, 20), BF (1, 5), B (1, 5), R (6, 30)
	GEN, KAN, AMK, TET, ERY, CIP, SYN	5 (1.5)	SW (3, 60), SuW (2, 40)
6	GEN, TET, ERY, CLI, CIP, MUPT	4 (1.2)	SuW (4, 100)
	GEN, TET, CIP, SXT, SYN, MUP	1 (0.3)	P (1, 100)
4	GEN, KAN, TET, ERY	17 (4.9)	SW (6, 35.3), BW (5, 29.4), P (4, 23.5), BF (1, 5.9), U (1, 5.9)
	GEN, TET, RIF, MUP	2 (0.6)	BW (1, 50), R (1, 50)
3	GEN, AMK, ERY	61 (17.7)	SW (21, 34.4), BW (11, 18.1), SuW (8, 13.1), P (8, 13.1), B (5, 8.2), U (5, 8.2), R (3, 4.9)
	GEN, TET, ERY	7 (2)	SW (4, 57.1), P (2, 28.6), U (1, 14.3)
1	TET	42 (12.2)	SW (7, 16.7), P (7, 16.7), U (14, 33.3), B (4, 9.5), R (10, 23.8)
Without resistance	—	36 (10.4)	SW (17, 47.2), P (17, 47.2), BF (2, 5.6)

AMK, amikacin; B, blood; BF, body fluid; BW, burn wounds; CIP, ciprofloxacin; CLI, clindamycin; ERY, erythromycin; GEN, gentamicin; KAN, kanamycin; P, purulent exudates; R, respiratory tract secretions; RIF, rifampin; SuW, surgical wounds; SW, skin wounds; SXT, trimethoprim/sulfamethoxazole; SYN, quinupristin/dalfopristin; TEC, teicoplanin; TET, tetracycline; TOB, tobramycin; U, urine.

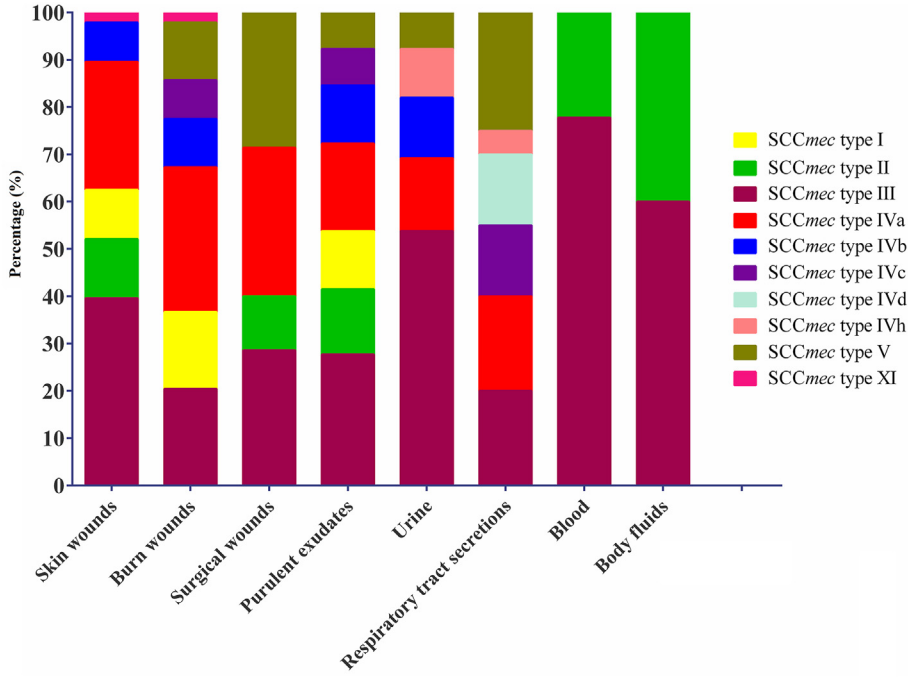

FIG. 1. Distribution of SCC*mec* types based on isolate sources.

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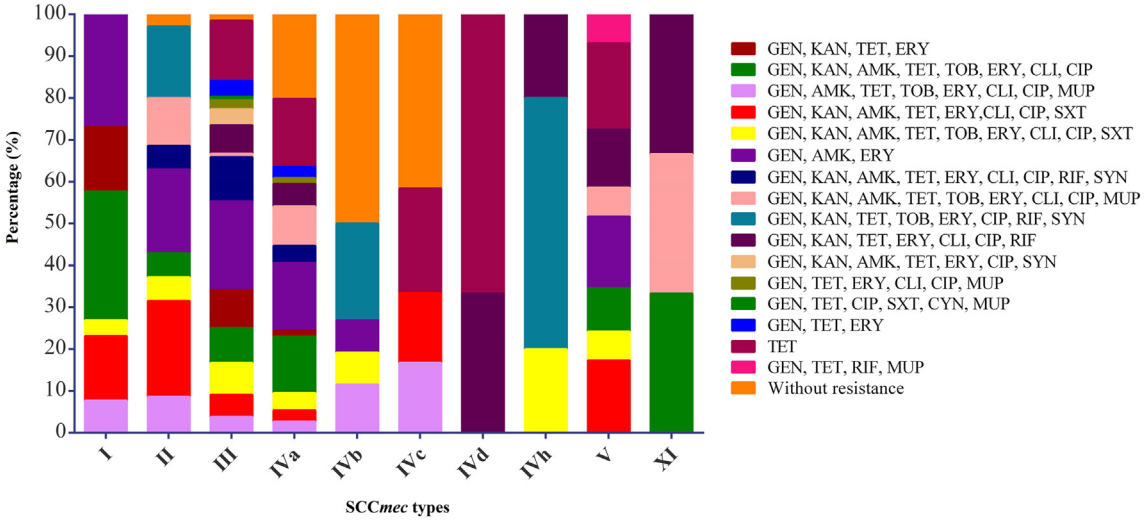

FIG. 2. Distribution of resistance profiles among different SCC*mec* types. AMK, amikacin; CIP, ciprofloxacin; CLI, clindamycin; ERY, erythromycin; GEN, gentamicin; KAN, kanamycin; RIF, rifampin; SXT, trimethoprim/sulfamethoxazole; SYN, quinupristin/dalfopristin; TET, tetracycline; TOB, tobramycin.

(0.9%) out of a total of 345 MRSA collected were positive for *mecC*. These *mecC* MRSA isolates were obtained from skin wounds (two isolates) and a burn wound (one isolate). Molecular typing showed that these isolates belonged to the clonal complex (CC)/ST130-*spa* type t843-*agr* type III (two isolates) and CC/ST599-*spa* type 5930-*agr* type I. All MRSA isolates harbouring the *mecC* gene carried SCC*mec* type XI and belonged to *coa* type III. The findings of the phenotypic evaluation of biofilm production in *mecC* MRSA isolates indicated that all isolates had strong ability to produce biofilm. The isolate belonging to CC/ST599 was positive for the *tst* gene. Information about characterization of the *mecC* MRSA isolates obtained from patients is summarized in Table 2.

Discussion

This report had several novel findings, including the first report concerning the detection of *mecC* MRSA in clinical samples in Iran. Strong biofilm formability with a predominance of *coa* type III in *mecC* MRSA strains was observed. A high prevalence of SCC*mec* type III was noted in MRSA isolates and highlights the role of these isolates in infection and outbreaks in healthcare settings. Different studies have addressed the importance and distribution of SCC*mec* types in understanding the origin of strains, the epidemiology and the clonal strain relatedness of MRSA [2,7,11,15].

Evidence indicates that hospital-associated (HA) and community-associated MRSA isolates may be related to different SCC*mec* types [3,4,15]. The distribution of SCC*mec* types in the 345 MRSA isolates showed that SCC*mec* type III was the most prevalent (38.3%), which emphasizes the nosocomial origin of these strains. This is in line with research conducted in the United States, Europe and most Asian countries [16–18]. SCC*mec* type III as the most prevalent cassette type was previously reported in studies conducted by Parhizgari *et al.* (95.7%) [17], Hashemizadeh *et al.* (28%) [19] and Ghanbari *et al.* (35.2%) [20] in Iran. According to our findings, SCC*mec* type III is

TABLE 2. Distribution of CCs, biofilm ability and molecular characterization of *mecC*-positive MRSA isolates

Strain	Genotype										
	Associated MLST CC	ST	*spa*	SCC*mec*	*agr*	*coa*	Toxin genes	Biofilm producer	Biofilm related genes	Antibiotic resistance	Resistance gene
IR1	130	130	t843	XI	III	III	—	Strong	*fnbA, fnbB, icaA, icaD, can*	GEN, KAN, AMK, TET, TOB, ERY, CLI, CIP, MUP	*mupA, tet*(M), *ant* (4′)-*Ia, aph* (3′)-*IIIa, msr*(B), *erm*(A)
IR2	130	130	t843	XI	III	III	—	Strong	*fnbA, fnbB, icaA, icaD, ebp*	GEN, KAN, AMK, TET, TOB, ERY, CLI, CIP	*ant* (4′)-*Ia, aph* (3′)-*IIIa, tet*(M), *msr*(B), *erm*(C),
IR3	599	599	5930	XI	I	III	*tst*	Strong	*fnbA, fnbB, icaD, icaA*	GEN, KAN, TET, ERY, CLI, CIP, RIF	*tet*(M), *ant* (4′)-*Ia, aac* (6′)-*Ie/aph* (2″), *erm*(C), *erm*(A)

AMK, amikacin; CC, clonal complex; CIP, ciprofloxacin; CLI, clindamycin; ERY, erythromycin; GEN, gentamicin; KAN, kanamycin; MLST, multilocus sequence typing; MRSA, methicillin-resistant *Staphylococcus aureus*; RIF, rifampin; ST, sequence type; SXT, trimethoprim/sulfamethoxazole; SYN, quinupristin/dalfopristin; TEC, teicoplanin; TET, tetracycline; TOB, tobramycin.

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responsible for most of the SCC*mec* types in HA-MRSA infections. Therefore, it is rational to speculate that high rates of this SCC*mec* type in the present study could be associated with the special lineage in Iran. On the basis of our previous observations, ST239-MRSA-III was the predominant ST among the HA-MRSA strains in Iran [10,11]. This evidence leads us to conclude that HA-MRSA strains collected in present survey may be linked to the ST239 clone. Similar to other studies [15,19–21], in the present study, cassette types I and II represented a minority, with frequencies of 7.5% and 10.1% respectively. Conversely, Chongtrakool *et al.* [22] studied 11 Asian countries and found that the most predominant SCC*mec* type among MRSA strains obtained from Korea and Japan was type II.

It is worth noting that some of the researchers documented the presence of SCC*mec* type IV in HA-MRSA and SCC*mec* type III in both HA- and community-associated MRSA, indicating their transfer from the community to hospitals and vice versa [3,4,15,21]. In the current study, SCC*mec* typing identified 83.3% of MRSA strains as type IV. This result is supported by the findings of Valsesia *et al.* [21] in Switzerland, who found SCC*mec* type IV to be the most frequent type among HA-MRSA strains (76.6%). A low prevalence, however, was noted for SCC*mec* types I (5%) and II (8.3%). Although the precise reason for the presence of SCC*mec* type IV strains in healthcare settings is unclear and of course debatable, it is well established that the growth of MRSA isolates with SCC*mec* type IV is more rapid and achieves a greater infectious burden than MRSA strains with other SCC*mec* types; therefore, they have a selective advantage [21]. Taken together, the strong presence of MRSA-IV and the considerable multidrug resistance in our hospital confirm the hypothesis of extensive transfer from the community to hospitals. Diversity in antibiotic susceptibility profiles was more prevalent among isolates with type III SCC*mec* than other SCC*mec* types. The same results have been reported from studies conducted by Moosavian *et al.* [15] and Hashemizadeh *et al.* [19].

The current study confirmed the presence of the *mecC* gene in three MRSA isolates with frequencies of 0.9%. To our knowledge, this is the first report regarding the emergence of the *mecC* gene in clinical MRSA strains from Iran. Similar to this study, studies from Denmark [23], Switzerland [24], France [25], the United Kingdom [26], Slovenia [27], Germany [28], Austria [29], Ireland [30] and Pakistan [31] have shown the presence of *mecC*-positive MRSA in both animal and human samples. Unlike other studies in which *mecC* MRSA isolates showed universal susceptibility to non–β-lactam antibiotics [8,26,29], this study showed the multidrug resistance pattern among these isolates.

Two of the three *mecC* MRSA in the present research belonged to the *agr* type III, *coa* type III, *spa* type t843 and CC/ST130. This finding is consistent with the observations of García-Álvarez *et al.* [7], who indicated that CC130 *mecC* MRSA is the most common lineage among human isolates in the United Kingdom and Denmark. Dermota *et al.* [27] in Slovenia analysed 395 MRSA strains isolated from different clinical samples from 2006 to 2013 and found six MRSA isolates harbouring the *mecC* gene, all of which belonged to CC/ST130. Dermota *et al.* also indicated that none of the MRSA isolates harbouring the *mecC* gene carried resistance genes and belonged to CC/ST130.

Although the occurrence of *mecC* in MRSA isolates belonging to ST599 was found to be rarely reported, we confirmed the presence of *tst*-positive CC/ST599 MRSA isolate harbouring the *mecC* gene with *spa* type 5930, *agr* type I and *coa* type III. Previously, the presence of CC/ST599 isolates was demonstrated in the United Kingdom, Austria, Belgium and Germany [5]. The current results regarding the toxin gene profile of ST599 isolates was similar to previously published ST599 MRSA isolates carrying the *mecC* gene [5,29]. This study was limited in that pulsed-field gel electrophoresis and DNA microarray techniques were not applied in the present work as a result of technical limitations.

In conclusion, this research depicted the first prevalence study of *mecC* MRSA in human samples in our area. This strain, however, does not seem to be highly prevalent in Iran. In this regard, routine detection approaches and molecular epidemiologic investigations of *mecC* MRSA are required to better understand the carriage, epidemiology and trends of this emerging human and animal pathogen.

Conflict of interest

None declared.

Acknowledgements

Supported financially by grant 20585 from the Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. The funding agency had no role in the design of the project, work execution, analyses, interpretation of the data, the writing of the report or the decision to submit.

References

[1] Troeman DP, Van Hout D, Kluytmans JA. Antimicrobial approaches in the prevention of *Staphylococcus aureus* infections: a review. J Antimicrob Chemother 2019;74:281–94.

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[2] Chukwunonso E, Veronica B, Toyo P, Chiagozie E, Amadi C, Abe T, et al. Methicillin-resistant *Staphylococcus aureus*: a mini review. Int J Med Res Health Sci 2018;7:122–7.
[3] Rasheed NA, Hussein NR. Methicillin-resistant *Staphylococcus aureus* carriage rate and molecular characterization of the staphylococcal cassette chromosome *mec* among Syrian refugees in Iraq. Int J Infect Dis 2020;91:218–22.
[4] Turlej AG, Hryniewicz WA, Empel J. Staphylococcal cassette chromosome *mec* (SCC*mec*) classification and typing methods: an overview. Pol J Microbiol 2011;60:95–103.
[5] Paterson GK, Harrison EM, Holmes MA. The emergence of *mecC* methicillin-resistant *Staphylococcus aureus*. Trends Microbiol 2014;22:42–7.
[6] Goudarzi M, Seyedjavadi SS, Azad M, Goudarzi H, Azimi H. Distribution of *spa* types, integrons and associated gene cassettes in *Staphylococcus aureus* strains isolated from intensive care units of hospitals in Tehran, Iran. Arch Clin Infect Dis 2016;11:e38813.
[7] García-Álvarez L, Holden MT, Lindsay H, Webb CR, Brown DF, Curran MD, et al. Meticillin-resistant *Staphylococcus aureus* with a novel *mecA* homologue in human and bovine populations in the UK and Denmark: a descriptive study. Lancet Infect Dis 2011;11:595–603.
[8] García-Garrote F, Cercenado E, Marín M, Bal M, Trincado P, Corredoira J, et al. Methicillin-resistant *Staphylococcus aureus* carrying the *mecC* gene: emergence in Spain and report of a fatal case of bacteraemia. J Antimicrob Chemother 2014;69:45–50.
[9] Yousefi M, Pourmand MR, Fallah F, Hashemi A, Mashhadi R, Nazari-Alam A. Characterization of *Staphylococcus aureus* biofilm formation in urinary tract infection. Iran J Publ Health 2016;45:485.
[10] Goudarzi M, Kobayashi N, Dadashi M, Pantůček R, Nasiri MJ, Fazeli M, et al. Prevalence, genetic diversity, and temporary shifts of inducible clindamycin resistance *Staphylococcus aureus* clones in Tehran, Iran: a molecular–epidemiological analysis from 2013 to 2018. Front Microbiol 2020;11:663.
[11] Ghaznavi-Rad E, Shamsudin MN, Sekawi Z, van Belkum A, Neela V. A simplified multiplex PCR assay for fast and easy discrimination of globally distributed staphylococcal cassette chromosome *mec* types in meticillin-resistant *Staphylococcus aureus*. J Med Microbiol 2010;59:1135–9.
[12] Harmsen D, Claus H, Witte W, Rothgänger J, Claus H, Turnwald D, et al. Typing of methicillin-resistant *Staphylococcus aureus* in a university hospital setting by using novel software for *spa* repeat determination and database management. J Clin Microbiol 2003;41:5442–8.
[13] Gilot P, Lina G, Cochard T, Poutrel B. Analysis of the genetic variability of genes encoding the RNA III-activating components *Agr* and TRAP in a population of *Staphylococcus aureus* strains isolated from cows with mastitis. J Clin Microbiol 2002;40:4060–7.
[14] Hirose M, Kobayashi N, Ghosh S, Paul SK, Shen T, Urushibara N, et al. Identification of staphylocoagulase genotypes I–X and discrimination of type IV and V subtypes by multiplex PCR assay for clinical isolates of *Staphylococcus aureus*. Jpn J Infect Dis 2010;63:257–63.
[15] Moosavian M, Shahin M, Navidifar T, Torabipour M. Typing of staphylococcal cassette chromosome *mec* encoding methicillin resistance in *Staphylococcus aureus* isolates in Ahvaz, Iran. New Microbe. New Infect 2018;21:90–4.
[16] Wang WY, Chiueh TS, Sun JR, Tsao SM, Lu JJ. Molecular typing and phenotype characterization of methicillin-resistant *Staphylococcus aureus* isolates from blood in Taiwan. PLoS One 2012;7:e30394.
[17] Parhizgari N, Khoramrooz SS, Malek Hosseini SA, Marashifard M, Yazdanpanah M, Emaneini M, et al. High frequency of multidrug-resistant *Staphylococcus aureus* with SCC *mec* type III and *spa* types t037 and t631 isolated from burn patients in southwest of Iran. APMIS 2016;124:221–8.
[18] Monecke S, Slickers P, Gawlik D, Müller E, Reissig A, Ruppelt-Lorz A, et al. Molecular typing of ST239-MRSA-III from diverse geographic locations and the evolution of the SCC*mec* III element during its intercontinental spread. Front Microbiol 2018;9:1436.
[19] Hashemizadeh Z, Hadi N, Mohebi S, Kalantar-Neyestanaki D, Bazargani A. Characterization of SCC*mec*, *spa* types and multi drug resistant of methicillin-resistant *Staphylococcus aureus* isolates among inpatients and outpatients in a referral hospital in Shiraz, Iran. BMC Res Notes 2019;12:614.
[20] Ghanbari F, Saberianpour S, Zarkesh-Esfahani FS, Ghanbari N, Taraghian A, Khademi F. Staphylococcal cassette chromosome *mec* (SCC*mec*) typing of methicillin-resistant *Staphylococcus aureus* strains isolated from community- and hospital-acquired infections. Avicenna J Clin Microbiol Infect 2017;4:42244.
[21] Valsesia G, Rossi M, Bertschy S, Pfyffer GE. Emergence of SCC*mec* type IV and SCC*mec* type V methicillin-resistant *Staphylococcus aureus* containing the Panton-Valentine leukocidin genes in a large academic teaching hospital in central Switzerland: external invaders or persisting circulators? J Clin Microbiol 2010;48:720–7.
[22] Chongtrakool P, Ito T, Ma XX, Kondo Y, Trakulsomboon S, Tiensasitorn C, et al. Staphylococcal cassette chromosome *mec* (SCC*mec*) typing of methicillin-resistant *Staphylococcus aureus* strains isolated in 11 Asian countries: a proposal for a new nomenclature for SCC*mec* elements. Antimicrob Agents Chemother 2006;50:1001–12.
[23] Petersen A, Stegger M, Heltberg O, Christensen J, Zeuthen A, Knudsen LK, et al. Epidemiology of methicillin-resistant *Staphylococcus aureus* carrying the novel *mecC* gene in Denmark corroborates a zoonotic reservoir with transmission to humans. Clin Microbiol Infect 2013;19:E16–22.
[24] Basset P, Prod'hom G, Senn L, Greub G, Blanc DS. Very low prevalence of meticillin-resistant *Staphylococcus aureus* carrying the *mecC* gene in western Switzerland. J Hosp Infect 2013;83:257–9.
[25] Laurent F, Chardon H, Haenni M, Bes M, Reverdy ME, Madec JY, et al. MRSA harboring *mecA* variant gene *mecC*, France. Emerg Infect Dis 2012;18:1465.
[26] Paterson GK, Morgan FJ, Harrison EM, Cartwright EJ, Török ME, et al. Prevalence and characterization of human *mecC* methicillin-resistant *Staphylococcus aureus* isolates in England. J Antimicrob Chemother 2014;69:907–10.
[27] Dermota U, Zdovc I, Strumbelj I, Grmek-Kosnik I, Ribic H, Rupnik M, et al. Detection of methicillin-resistant *Staphylococcus aureus* carrying the *mecC* gene in human samples in Slovenia. Epidemiol Infect 2015;143:1105–8.
[28] Cuny C, Layer F, Strommenger B, Witte W. Rare occurrence of methicillin-resistant *Staphylococcus aureus* CC130 with a novel *mec* A homologue in humans in Germany. PLoS One 2011;6:e24360.
[29] Kerschner H, Harrison EM, Hartl R, Holmes MA, Apfalter P. First report of *mecC* MRSA in human samples from Austria: molecular characteristics and clinical data. New Microbe. New Infect 2015;3:4–9.
[30] Shore AC, Deasy EC, Slickers P, Brennan G, O'Connell B, Monecke S, et al. Detection of staphylococcal cassette chromosome *mec* type XI carrying highly divergent *mecA*, *mecI*, *mecR1*, *blaZ*, and *ccr* genes in human clinical isolates of clonal complex 130 methicillin-resistant *Staphylococcus aureus*. Antimicrob Agents Chemother 2011;55:3765–73.
[31] Khan AA, Ali A, Tharmalingam N, Mylonakis E, Zahra R. First report of *mecC* gene in clinical methicillin resistant *S. aureus* (MRSA) from tertiary care hospital Islamabad, Pakistan. J Infect Publ Health 2020.

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