



High frequency of SCCmec type IV and multidrug-resistant SCCmec type I among hospital acquired methicillin-resistant Staphylococcus aureus isolates in Birjand Imam Reza Hospital, Iran

Toktam Sadeghi Moghaddam¹, Mohammad Hasan Namaei², Davoud Afshar³, Masoud Yousefi^{2*}

¹Student Research Committee, Birjand University of Medical Sciences, Birjand, Iran ²Infectious Diseases Research Center, Birjand University of Medical Sciences, Birjand, Iran ³Department of Microbiology and Virology, School of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran

Received: July 2021, Accepted: December 2021

ABSTRACT

Background and Objectives: The ever-increasing of antibiotic resistance in methicillin-resistant Staphylococcus aureus (MRSA) has become a major threat to public health worldwide. Molecular typing is used to determine the source of MRSA infections as well as to control and prevent the spread of these pathogens. The present study aimed to investigate the characteristics of staphylococcal cassette chromosome mec (SCCmec) types and antibiotic resistance of community- acquired (CA-) and hospital acquired (HA-) MRSA isolates.

Materials and Methods: In this cross-sectional study, the antibiotic susceptibility patterns of 109 clinical S. aureus isolates were determined by the Kirby-Bauer disk-diffusion and microdilution broth methods. MRSA isolates were confirmed using the polymerase chain reaction (PCR) method for the detection of the mecA gene. SCCmec typing was performed by a multiplex PCR assay among MRSA isolates.

Results: The prevalence of MRSA isolates was 39.4%. Linezolid, vancomycin, and ceftaroline were the most effective agents against MRSA isolates. The incidence of multidrug-resistant (MDR) and resistance to most antibiotics were significantly higher in MRSA than methicillin-susceptible S. aureus (MSSA) isolates (P<0.05). SCCmec types I, III, and IV were identified in 27.9%, 23.3%, and 37.2% of MRSA isolates, respectively. SCCmec type I and IV were the most prevalent SCCmec types in HA-MRSA isolates (each was 32.4%). While SCCmec type IV (66.7%) was the most frequently SCCmec type associated with CA-MRSA isolates.

Conclusion: Our findings demonstrated a high rate of MDR among MRSA isolates. The high existence of SCCmec type IV was reported among the HA-MRSA isolates, which can indicate the spread of MRSA community isolates to hospital settings. Therefore, appropriate antibiotic stewardship plans and microbiological surveillance initiatives must be implemented in healthcare facilities to monitor and limit the spread of these resistant bugs.

Keywords: Methicillin-resistant Staphylococcus aureus; Drug resistance; Multidrug-resistant; mecA gene; Molecular typing; Polymerase chain reaction

*Corresponding author: Masoud Yousefi, Ph.D, Infectious Diseases Research Center, Birjand University of Medical Sciences, Birjand, Iran Tel: +98-5632381518 Fax: +98-5632381509 Email: Masoud.yousefi@bums.ac.ir



Copyright © 2022 The Authors. Published by Tehran University of Medical Sciences.

This work is licensed under a Creative Commons Attribution-Non Commercial 4.0 International license (https://creativecommons.org/licenses/by-nc/4.0/). Noncommercial uses of the work are permitted, provided the original work is properly cited.

INTRODUCTION

Staphylococcus aureus is one of the most frequent pathogens in community and health care facilities and is considered as a serious threat to human health. This pathogen is responsible for a wide range of diseases from folliculitis to food poisoning, as well as causing life-threatening infections such as bacteremia, endocarditis, necrotizing pneumonitis, and osteomyelitis (1, 2).

The emergence of methicillin-resistant *S. aureus* (MRSA) strains has become an increasing health concern worldwide. The potential for genetic adaptation and the remarkable ability of MRSA strains to acquire resistance to multiple antimicrobials complicated the treatment of related infections. Therefore, a major public health concern still remains with respect to the high morbidity and mortality of infections caused by MRSA, along with increased hospitalization and health care costs (3, 4).

Although MRSA infections were originally acquired only from hospital settings (HA-MRSA), outbreaks of infection in the community were first reported in the 1990s. However, CA-MRSA infections are now increasingly spreading in hospital settings and are replacing traditional HA-MRSA strains (2, 5). Since antibiotic management and virulence properties of CA-MRSA strains are different from HA-MRSA, it can be important to identify and differentiate the bacteria to reduce unnecessary suffering, the length of hospital stay, and healthcare costs for affected patients (6, 7).

The staphylococcal cassette chromosome *mec* (SCC*mec*) mobile element carries both the *mecA* or *mecC* genes that mediate resistance to methicillin in *S. aureus* (8, 9). To date, thirteen different types of SCC*mec* elements (SCC*mec* I-XIII) have been identified based on structural organization and genetic content, and each SCC*mec* type has individual characteristics (4, 10). Noteworthy, SCC*mec* types I, II, and III are the most seen types found in hospital acquired MRSA (HA-MRSA), whereas types IV and V are prominent SCC*mec* types among community-acquired MRSA (CA-MRSA) strains (11, 12).

Given the importance of global surveillance studies on resistance profiles and epidemiological types of MRSA strains, along with the current challenges in the treatment of infections caused by these pathogens, the present study aimed to investigate the characteristics of SCC*mec* types and antibiotic resistance of CA- and HA-MRSA isolates in Birjand Imam Reza hospital, Iran.

MATERIALS AND METHODS

Study design and bacterial isolation. This cross-sectional study was conducted on a total of 109 non-duplicate clinical *S. aureus* isolates collected from out-patients and in-patients (hospital stay >48 hours at the time of specimen collection) referred to Birjand Imam Reza Hospital in Iran from Mar 2018 to Feb 2019. The clinical samples contained urine, joint fluids, lung secretions, wound swab, ear secretions, ascetic fluid, and other samples. The study was approved by the ethics committee of Birjand University of Medical Sciences (IR.BUMS. REC.1396.110).

S. aureus isolates were identified using conventional microbiological methods, such as evaluation of colony morphology on sheep blood agar, Gram-staining, catalase activity, production of coagulase, DNase test (Merck, Germany), and mannitol fermentation on mannitol salt agar (Merck, Germany).

Antibiotic susceptibility testing (AST). The antibiotic resistance profile of the isolates was determined according to the Clinical and Laboratory Standards Institute (CLSI) guidelines (13). The Kirby-Bauer disk-diffusion method was used for susceptibility testing to erythromycin (15 µg), clindamycin (2 µg), doxycycline (30 µg), gentamicin (10 µg), tetracycline (30 µg), ciprofloxacin (5 µg), rifampin (5 μg), trimethoprim /sulfamethoxazole (1.25/23.75 μg), ceftaroline (30 µg), linezolid (30 µg) and quinupristin/dalfopristin (15 µg) (MAST, UK). Furthermore, the minimum inhibitory concentration (MIC) value of vancomycin (Sigma-Aldrich, USA) against the isolates was determined by the microdilution broth method. S. aureus ATCC 25923 and S. aureus ATCC 29213 were used for quality control of antibiotic susceptibility testing.

Screening of methicillin-resistant *S. aureus* (MRSA). MRSA strains were identified phenotypically using the cefoxitin disk diffusion method (30 μ g; MAST, UK) according to the CLSI guidelines (13). *S. aureus* isolates with an inhibition zone diameter of \leq 21mm around the cefoxitin disk were confirmed as MRSA strain.

Detection of mecA gene. The existence of the *mecA* gene in all MRSA isolates was determined employing PCR assay with specific primers described in Table 1. Genomic DNA was extracted from pure cultures of the isolates using a High Pure PCR Template Preparation Kit (Roche, Germany) according to the manufacturer's instructions. The PCR amplification for the *mecA* gene was carried out as described previously (14). The amplified products were electrophoresed on 1% agarose gel containing 1× RedSafe DNA stain (Intron, USA).

SCCmec typing. In this study, a multiplex PCR assay with specific primers (Table 1) described by Boye and colleagues (15) was developed to SCCmec typing (SCCmec type I-V) among MRSA isolates harboring the mecA gene. Amplification of SCCmec genes was performed in a final volume of 25 mL consisting of 12.5 µl of 2× Hot Star Taq Master Mix (Amplicon, Denmark), 3 µl of the DNA template, an optimized amount of each primer with a concentration of 10 pmol/ μ L (0.5 μ l of each β , α 3, ccrCF, and ccrCR; 0.3 µl of each 1272F1, 1272R1, 5RmecA, and 5R431), and 6.3 µl of ddH2O. DNA amplification was performed in a thermocycler (PEQLAB, Erlangen, Germany) with an initial denaturation step at 94°C for 4 minutes; 30 amplification cycles each for 45 seconds at 94°C, 30 seconds at 55°C, and 1 minute at 72°C; and followed by an additional extension step of 5 minutes at 72°C. The amplified products were electrophoresed on 1.5% agarose gel containing 1× RedSafe DNA stain (Intron, USA). Noteworthy, the SCCmec types were determined based upon the results of the obtained band pattern comparing to ATCC 10442 (SCCmec type I), N315 (SCCmec type II), 85/2082 (SCCmec type III), MW2 (SCCmec type IVa), and

Table 1. Target genes and their primers used in this study.

WIS (SCC*mec* type V), as reference strains. Isolates with no visible bands, or with a band pattern that was not in agreement with one of the five predicted band patterns, were classified as non-typeable (NT).

Statistical analysis. The data were analyzed with the Pearson chi-square and Fisher's exact tests, using SPSS software (version 21), to evaluate the statistical significance of associations between potential variables. P-values of less than 0.05 were regarded as statistically significant.

RESULTS

Out of the total 109 *S. aureus* isolates isolated from different clinical samples, the majority of the isolates were originated from wound swabs (33 isolates, 36%), followed by lung secretions (27 isolates, 24.8%), urine (25 isolates, 22.9%), ear secretions (10 isolates, 9.2%), ascetic fluid (Two isolates, 1.8%), and joint fluids (One isolate, 0.9%).

Among the 109 isolates obtained, 67 (61.5%) were from males and 42 (38.5%) were from females. The mean age of patients was 32.12 ± 16.51 years old (range of 1-78 years), of which 72 (66.1%) were hospitalized and 37 (33.9%) were out-patients.

Antibiotic resistance characteristics. The results of the antimicrobial resistance determinations of *S. aureus* isolates are reported in Table 2. The findings showed a high susceptibility of the isolates to linezolid (100%), vancomycin (100%), ceftaroline (99.1%), and quinupristin/dalfopristin (88.1%). In the present study, 48 *S. aureus* isolates (44%, 48/109) were identified as multidrug-resistant (MDR) that these MDR

	Primers	Sequence (5'-3')	Products sizes (bp)	Annealing (°C)	Ref.
SCCmec Typing	mecA	Fw-TGGCTATCGTGTCACAATCG	304	58	(14)
		Rv- CTGGAACTTGTTGAGCAGAG			
	β	ATTGCCTTGATAATAGCCYTCT	937		
	α.3	TAAAGGCATCAATGCACAAACACT			
	ccrCF	CGTCTATTACAAGATGTTAAGGATAAT	518	55	(15)
	ccrCR	CCTTTATAGACTGGATTATTCAAAATAT			
	1272F1	GCCACTCATAACATATGGAA	415		
	1272R1	CATCCGAGTGAAACCCAAA			
	5RmecA	TATACCAAACCCGACAACTAC	359		
	5R431	CGGCTACAGTGATAACATCC			

TOKTAM SADEGHI MOGHADDAM ET AL.

S. aureus isolates (52.8% vs. 27%, P=0.01) were significantly more common in hospitalized patients than in out-patients.

In the present study, the prevalence of methicillin-susceptible *S. aureus* (MSSA) and MRSA isolates was 60.6% (66/109) and 39.4% (43/109), respectively. Statistical analysis indicated that resistance to most antibiotics such as erythromycin (44.2% vs. 16.7%, P=0.003), rifampin (39.5% vs. 10.6%, P=0.001), quinupristin/dalfopristin (25.6% vs. 3%, P=0.001), clindamycin (55.8% vs. 4.5%, P=0.0001), doxycycline (20.9% vs. 7.6%, P=0.015), gentamicin (30.2% vs. 10.6%, P=0.017), tetracycline (58.1% vs. 25.8%, P=0.001), and ciprofloxacin (39.5% vs. 15.2%, P=0.016) was significantly higher in MRSA than MSSA isolates. Noteworthy, the incidence of MDR in MRSA isolates was significantly (P<0.001) higher than MSSA isolates, 81.4% vs. 19.7%, respectively.

The infection rate of MRSA isolates (51.4% vs. 16.2%, P=0.0001) was shown to be significantly higher in in-patients (HA) compared with out-patients (CA). Comparison of resistance pattern of HA-MR-SA and CA-MRSA strains to antimicrobial agents is shown in Table 2. The findings revealed that resistance to quinupristin/dalfopristin (29.7% vs. 0%, P=0.018),

and clindamycin (62.2% vs. 16.7%, P=0.037) was considerably higher in HA-MRSA compared to CA-MRSA strains. Finally, among CA- and HA-MR-SA, 66.7 percent (4/6) and 81.1 percent (30/37) were found to be MDR, respectively (P=0.369).

SCCmec typing patterns. In the present study, the mecA gene was found in all MRSA isolates. Out of 43 mecA positive isolates, SCCmec types I, III, and IV were identified in 12 (27.9%), 10 (23.3%), and 16 (37.2%) of MRSA isolates, respectively, and five (11.6%) isolates were not typeable. The PCR amplification of products obtained from SCCmec typing of MRSA isolates is shown in Fig. 1. Noteworthy, SCCmec type I and IV were the most prevalent SCCmec types in HA-MRSA isolates (each was 32.4%). While SCCmec type IV (66.7%) was the most frequently SCCmec type associated with CA-MRSA isolates (Table 3). In this study, statistical analysis did not show a significant difference in the frequency of SCCmec types between HA-MRSA and CA-MRSA isolates (P>0.05).

The antimicrobial resistance patterns of MRSA isolates grouped by SCC*mec* types are summarized in Table 4. The findings showed high resistance to most

Table 2. Resistance pattern of S. aureus and MRSA isolates to different antimicrobial agents.

Antimicrobial Agents S. aureus Methicillin-resistant Status MRSA isolates isolates (%) MRSA(%) MSSA(%) P-value HA-MRSA (%) CA-MRSA (%) P-value Erythromycin (n=43)(n=37) (n=66)(n=6)Ceftaroline 30 (27.5) 11 (16.7) 0.003 18 (48.6) 1 (16.7) 0.341 19 (44.2) Rifampin 1 (0.9) 0(0)0.394 0(0)0.860 1 (2.3) 1 (2.7) Trimethoprim/sulfamethoxazole 0.001 23 (21.1) 17 (39.5) 7 (10.6) 10(27) 1 (16.7) 0.696 Quinupristin 20 (18.3) 11 (25.6) 9 (13.6) 0.243 /dalfopristin 0.018 13 (11.9) 11 (25.6) 2(3)0.001 11 (29.7) 0(0)Clindamycin 27 (24.8) 24 (55.8) 3(4.5)0.0001 23 (62.2) 1 (16.7) 0.037 Doxycycline 14 (12.8) 9 (20.9) 5 (7.6) 0.015 8 (21.6) 1 (16.7) 0.64 Gentamicin 20 (18.3) 13 (30.2) 7 (10.6) 0.017 12 (32.4) 1 (16.7) 0.274 Tetracycline 42 (38.5) 25 (58.1) 17 (25.8) 0.001 23 (62.2) 2 (33.3) 0.344 Ciprofloxacin 27 (24.8) 17 (39.5) 10 (15.2) 0.016 14 (37.8) 3 (50) 0.224 0(0)Cefoxitin 43 (39.4) 66 (100) NA NA NA NA Linezolid 0(0)0(0)0(0)NA 0(0) 0(0)NA Vancomycin 0(0) 0(0)0(0)0(0)0(0)NA NA MDR Status Yes 48 (44) 35 (81.4) 13 (19.7) < 0.001 30 (81.1) 4 (66.7) 0.369 61 (56) 8 (18.6) 53 (80.3) 7 (18.9) 2 (33.3) No

MDR: Multidrug-resistant, MRSA: Methicillin-resistant *S. aureus*, MSSA: Methicillin-susceptible *S. aureus*, HA-MRSA: Hospital-acquired MRSA, CA-MRSA: Community-acquired MRSA, NA: Not applicable.



Fig. 1. PCR amplification of products obtained from SCC*mec* typing of MRSA isolates. Lane 1 and 6, DNA marker (100 bp); Lane 2, Clinical MRSA SCC*mec* type I strain (415 bp); Lane 3, Clinical MRSA SCC*mec* type III strain (518 bp); Lane 4, Clinical MRSA SCC*mec* type IV strain (415 and 937 bp); Lane 5, Negative control; Lane 7, *S. aureus* WIS 173 (SCC*mec* type V); Lane 8, *S. aureus* N315 strain (SCC*mec* type II).

antibiotics in MRSA with type III SCC*mec*. So that, the MRSA SCC*mec* type III strains were significantly more resistant to rifampin (P=0.025), gentamicin (P=0.007), tetracycline (P=0.043), and ciprofloxacin (P=0.01) than strains with other types of SCC*mec*. Furthermore, all MRSA SCC*mec* type III strains were identified as MDR (100%). In contrast, compared with SCC*mec* I/III MRSA strains, a greater proportion of SCC*mec* IV strains were susceptible to most antibiotics tested. The results indicated that the MRSA SCC*mec* type IV strains were more multidrug-susceptible compared to the other SCC*mec* types.

DISCUSSION

Today, the emergence of MRSA isolates has become a major challenge in public health. MRSA isolates are commonly MDR strains, and this issue can

Table 3. Distribution of SCCmec types among CA- and HA-MRSA isolates.

SCCmec	MRSA	P-value	
Types	HA-MRSA (%)		
	(n=37)	(n=6)	
Ι	12 (32.4)	0 (0)	0.121
III	9 (24.3)	1 (16.7)	0.571
IV	12 (32.4)	4 (66.7)	0.125
NT	4 (10.8)	1 (16.7)	0.547

MRSA: Methicillin-resistant *S. aureus*, HA-MRSA: Hospital-acquired MRSA,

CA-MRSA: Community- acquired MRS, NT: Non-typeable.

lead to limited therapeutic options for the control of infections, causing high morbidity and mortality, especially in hospitalized patients (3, 10).

In the current study, the prevalence of MRSA isolates was 39.4%, which is almost consistent with some studies in Iran (8, 10, 16, 17), and other countries such as the Philippines (45.76%), India (35.33%), Iraq (42.5%), Pakistan (39%), Africa (53.4%), Nigeria (41.4%), and Brazil (33.3%) (7, 18-22). However, there are reports of much higher rates of MRSA isolates compared with our study from several other studies in Iran (12, 23-25), and Sudan (70%), Sweden (70%), Nepal (75%), USA (75%), and India (93.5%) (26-30). These discrepancies in the prevalence of MRSA isolates could be explained by differences in the studied patients, the clinical samples, the geographic areas, the infection-control policies, and the diagnostic techniques.

The findings revealed that resistance to tetracycline (58.1%), clindamycin (55.8%), erythromycin (44.2%), and ciprofloxacin and rifampin (each was 39.5%) was the most common resistance pattern among MRSA isolates. Moreover, 81.4% of MRSA isolates were identified as MDR. This pattern of antibiotic resistance is in line with the results of many studies. Japoni et al. demonstrated a reduced gradient of MRSA susceptibility to rifampin, co-trimoxazole, clindamycin, tetracycline, ciprofloxacin, and erythromycin (31). In another study, the highest resistance of MRSA isolates was related to levofloxacin, ciprofloxacin, erythromycin, and clindamycin (9). In the study of Rossato and colleagues, the highest levels of resistance among MRSA isolates were reported against erythromycin, ciprofloxacin, and clindamy-

TOKTAM SADEGHI MOGHADDAM ET AL.

Antimicrobial Agents	SCCmec Types			P-value	
	I (%)	III (%)	IV (%)	NT (%)	
	n=12	n=10	n=16	n=5	
Erythromycin	4 (33.3)	7 (70)	4 (25)	4 (80)	0.137
Ceftaroline	0 (0)	0 (0)	0 (0)	1 (20)	0.051
Rifampin	3 (25)	8 (80)	4 (25)	2 (40)	0.025
Trimethoprim /sulfamethoxazole	4 (33.3)	1 (10)	4 (25)	2 (40)	0.665
Quinupristin/dalfopristin	3 (25)	3 (30)	3 (18.8)	2 (40)	0.857
Clindamycin	7 (58.3)	8 (80)	5 (31.3)	4 (80)	0.057
Doxycycline	1 (8.3)	3 (30)	3 (18.8)	2 (40)	0.315
Gentamicin	1 (8.3)	7 (70)	2 (12.5)	3 (60)	0.007
Tetracycline	9 (75)	9 (90)	5 (31.3)	2 (40)	0.043
Ciprofloxacin	1 (8.3)	8 (80)	4 (25)	4 (80)	0.01
MDR Status					
Yes	10 (83.3)	10 (100)	10 (62.5)	5 (100)	0.065
No	2 (16.7)	0 (0)	6 (37.5)	0 (0)	

Table 4. Distribution of antimicrobial resistance among MRSA isolates by SCCmec types characteristics.

MDR: Multidrug-resistant, NT: Non-typeable.

cin (4). Nevertheless, in many studies in line with our study, vancomycin, linezolid, and ceftaroline were introduced as the most effective antibiotics against MRSA isolates (16, 20, 31-33).

In this study, the rates of antibiotics resistance in MRSA isolates were higher in comparison with MSSA isolates. The results indicated that resistance to most antibiotics such as erythromycin, rifampin, quinupristin/dalfopristin, clindamycin, doxycycline, gentamicin, tetracycline, and ciprofloxacin was significantly higher in MRSA than MSSA isolates. Noteworthy, the incidence of MDR in MRSA isolates. Many studies in line with our study have reported high antibiotic resistance of MRSA isolates to MSSA (10, 33-35). Hence, the accurate identification and reporting of MRSA isolates would help select the appropriate antibiotic therapy and, control and minimize the spread of these MDR isolates.

In humans, bacterial infections from MRSA have been acknowledged for several years as either HA-MRSA or CA-MRSA depending on the source of infection. CA-MRSA strains have been found to have distinctive genetic composition, antimicrobial characteristics, and virulence properties that set them apart from HA-MRSA strains. Clinically, HA-MRSA strains are usually MDR and the infections caused by them are associated with high morbidity and mortality (2, 7, 17). In the present study, the infection rate of MRSA isolates (51.4% vs. 16.2%, P=0.0001) was shown to be significantly higher in in-patients (HA) compared with out-patients (CA). A similar result was reported by Preeja et al. where the prevalence of MRSA among in-patients and out-patients was 96.1% and 55.6%, respectively. Furthermore, a significant difference was observed between the isolation of HA-MRSA and CA-MRSA from the inpatient and outpatient groups (2). In another study, the incidence of HA-MRSA and CA-MRSA infection was reported to be 73% and 37%, respectively (23). In the study of Tsige and colleagues, the frequency of MRSA isolates in in-patients (19.5%) was higher as compared to out-patient (5.4%) (36). It is noteworthy that in our study, the resistance to most antibiotics in HA-MRSA strains was higher than CA-MRSA so that this difference was significant for quinupristin/ dalfopristin (29.7% vs. 0%, P=0.018) and clindamycin (62.2% vs. 16.7%, P=0.037). Moreover, among CA- and HA-MRSA, 66.7% and 81.1% were found to be MDR, respectively. These findings are in line with the results of many studies that have reported high antibiotic resistance in HA-MRSA strains compared to CA-MRSA (2, 11, 18, 35). Overall, it should be noted that the high occurrence of MRSA isolates with high rates of resistance to commonly used antimicrobials among hospitalized patients is not surprising due to various hospital-related factors such as long-term hospitalization, the use of various

antibiotics for treatment, and underlying immunodeficiency conditions, which predispose patients to acquire MRSA.

Nowadays, applying a simple, rapid and accurate typing method can help identify the source of antibiotic-resistant infections. SCCmec typing provides useful information about antimicrobials resistance, and to determine the epidemiological relationship between various MRSA strains and origin of infection (3, 10). In the current study, the most prevalent SCCmec types among MRSA isolates was SCCmec IV (37.2%), followed by SCCmec I (27.9%), and SCCmec III (23.3%). Similar results in some studies indicate the predominance of type SCCmec IV in MRSA isolates (3, 4, 7, 10, 37), which can be explained by the fact that the small size of this SCCmec type may facilitate its spread among MRSA isolates collected from hospitals and communities (10, 38). Noteworthy, SCCmec type I and IV were the most prevalent SCCmec types in HA-MRSA isolates (each was 32.4%) in our study. While, SCCmec type IV (66.7%) was the most frequently SCCmec type associated with CA-MRSA isolates. In this regard, some studies have shown a high prevalence of SCCmec type IV among the HA-MRSA isolates (2, 10, 11, 23), which can indicate that the MRSA community isolates has spread to the hospital settings. Therefore, applying an action plan with appropriate antibiotic stewardship and the implementation of strict aseptic techniques can help control colonization and the spread of CA-MRSA isolates to health care facilities. Finally, the findings of current study showed a high resistance to most antibiotics in MRSA with types I and III SCCmec, while a greater proportion of SCCmec IV strains were susceptible to most antibiotics. Similar results have been found in many previous studies (4, 16, 17, 39), and this is because SCCmec types I and III is often observed in HA-MRSA isolates, which generally has a high antibiotic resistance.

CONCLUSION

Our findings demonstrated a high rate of MDR among MRSA isolates. In this study, linezolid, vancomycin, and ceftaroline were still effective antibiotics to treat MRSA infections. The present results showed the high existence of SCC*mec* type IV among the HA-MRSA isolates, which can indicate the spread of MRSA community isolates to hospital settings. It is imperative that appropriate antibiotic stewardship plans and microbiological surveillance initiatives are implemented in healthcare facilities to monitor and limit the spread of these resistant bugs.

ACKNOWLEDGEMENTS

This research was supported by Birjand University of Medical Sciences, Birjand, Iran (grant number 455288).

REFERENCES

- Neupane K, Rayamajhee B, Acharya J, Rijal N, Shrestha D, GC B, et al. Comparison of nasal colonization of methicillin-resistant *Staphylococcus aureus* in HIV-infected and non-HIV patients attending the national public health laboratory of Central Nepal. *Can J Infect Dis Med Microbiol* 2018; 2018: 4508757.
- Preeja PP, Kumar SH, Shetty V. Prevalence and Characterization of methicillin-resistant *Staphylococcus aureus* from community-and hospital-associated infections: a tertiary care center study. *Antibiotics (Basel)* 2021; 10: 197.
- 3. Moshtagheian S, Halaji M, Sedaghat H, Shahin M, Esfahani BN, Havaei SR, et al. Molecular characteristics of methicillin-resistant *Staphylococcus aureus* nasal carriage from hospitalized patients and medical staff in Isfahan, Iran. *Ann Ig* 2018; 30: 237-244.
- Rossato AM, Primon-Barros M, Rocha LDL, Reiter KC, Dias CAG, d'Azevedo PA. Resistance profile to antimicrobials agents in methicillin-resistant *Staphylococcus aureus* isolated from hospitals in South Brazil between 2014-2019. *Rev Soc Bras Med Trop* 2020; 53:e20200431.
- Rahimi F, Katouli M, Karimi S. Biofilm production among methicillin resistant *Staphylococcus aureus* strains isolated from catheterized patients with urinary tract infection. *Microb Pathog* 2016; 98: 69-76.
- Barnes BE, Sampson DA. A literature review on community-acquired methicillin-resistant *Staphylococcus aureus* in the United States: clinical information for primary care nurse practitioners. J Am Acad Nurse Pract 2011; 23: 23-32.
- Valle DL Jr, Paclibare PA, Cabrera EC, Rivera WL. Molecular and phenotypic characterization of methicillin-resistant *Staphylococcus aureus* isolates from a tertiary hospital in the Philippines. *Trop Med Health* 2016; 44: 3.
- 8. Tajik S, Najar-Peerayeh S, Bakhshi B, Golmohammadi

R. Molecular characterization of community-associated methicillin-resistant *Staphylococcus aureus* in Iranian burn patients. *Iran J Pathol* 2019; 14: 284-289.

- Kot B, Wierzchowska K, Piechota M, Grużewska A. Antimicrobial resistance patterns in methicillin-resistant *Staphylococcus aureus* from patients hospitalized during 2015–2017 in hospitals in Poland. *Med Princ Pract* 2020; 29: 61-68.
- Hashemizadeh Z, Hadi N, Mohebi S, Kalantar-Neyestanaki D, Bazargani A. Characterization of SCCmec, 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.
- Ahmadishoar S, Pour NK, Sadeghi J, Nahaei MR, Kheirkhah B. Genotypic and phenotypic characterisation of clinical isolates of methicillin-resistant *Staphylococcus aureus* in two different geographical locations of Iran. Indian *J Med Microbiol* 2020; 38: 162-168.
- Momtaz H, Hafezi L. Meticillin-resistant *Staphylococ*cus aureus isolated from Iranian hospitals: virulence factors and antibiotic resistance properties. *Bosn J Basic Med Sci* 2014; 14: 219-226.
- Wayne P .(2019) Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing. 29th ed. CLSI supplement M100S.
- Alipour F, Ahmadi M, Javadi S. Evaluation of different methods to detect methicillin resistance in *Staphylococcus aureus* (MRSA). *J Infect Public Health* 2014; 7: 186-191.
- Boye K, Bartels MD, Andersen IS, Møller JA, Westh H. A new multiplex PCR for easy screening of methicillin-resistant *Staphylococcus aureus* SCCmec types I–V. Clin Microbiol Infect 2007; 13: 725-727.
- 16. Fatholahzadeh B, Emaneini M, Gilbert G, Udo E, Aligholi M, Modarressi MH, et al. Staphylococcal cassette chromosome *mec* (SCC *mec*) analysis and antimicrobial susceptibility patterns of methicillin-resistant *Staphylococcus aureus* (MRSA) isolates in Tehran, Iran. *Microb Drug Resist* 2008; 14: 217-220.
- 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 Microbes New Infect* 2018; 21: 90-94.
- Bhutia KO, Singh T, Adhikari L, Biswas S. Molecular characterization of community-& hospital-acquired methicillin-resistant & methicillin-sensitive *Staphylococcus aureus* isolates in Sikkim. *Indian J Med Res* 2015; 142: 330-335.
- 19. Hussain S, Shams R, Ahmad K, Perveen R, Riaz B. Prevalence of methicillin resistant *Staphylococcus aureus* (MRSA) in surgical site infections in a tertiary

care hospital. Int J Pathol 2005; 3: 81-85.

- Wangai FK, Masika MM, Maritim MC, Seaton RA. Methicillin-resistant *Staphylococcus aureus* (MRSA) in East Africa: red alert or red herring?. *BMC Infect Dis* 2019; 19: 596.
- Terry Alli OA, Ogbolu DO, Mustapha JO, Akinbami R, Ajayi AO. The non-association of Panton-Valentine leukocidin and *mecA* genes in the genome of *Staphylococcus aureus* from hospitals in South Western Nigeria. *Indian J Med Microbiol* 2012; 30: 159-164.
- 22. Rodrigues MdA, Gindri L, Silva ADd, Guex CG, Santos SOd, Hörner R. Prevalence of methicillin-resistant *Staphylococcus aureus* in a university hospital in the south of Brazil. *Braz J Pharm Sci* 2015; 51: 35-41.
- 23. Fasihi Y, Kiaei S, Kalantar-Neyestanaki D. Characterization of SCCmec and spa types of methicillin-resistant *Staphylococcus aureus* isolates from health-care and community-acquired infections in Kerman, Iran. J Epidemiol Glob Health 2017; 7: 263-267.
- 24. Afsharian M, Hemmati M, Mansouri F, Azizi M, Zamanian MH, Mohseni Afshar Z, et al. Frequency of class I and II integrons in methicillin-resistant and methicillin-sensitive *Staphylococcus aureus* isolates in the City of Kermanshah. *Arch Clin Infect Dis* 2019; 14(4); e86688.
- 25. Motallebi M, Jabalameli F, Beigverdi R, Emaneini M. High prevalence of direct repeat unit types of 10di, 8 h and 8i among methicillin resistant *Staphylococcus aureus* strains with staphylococcal cassette chromosome mec type IIIA isolated in Tehran, Iran. *Antimicrob Resist Infect Control* 2019; 8: 50.
- 26. Moglad EH. Prevalence of methicillin-resistant *Staph-ylococcus aureus* (MRSA) in clinical specimens and among hospital staff nasal carriers in khartoum state. *Int J Pharm Sci Res* 2021; 12; 673-677.
- Gurung RR, Maharjan P, Chhetri GG. Antibiotic resistance pattern of *Staphylococcus aureus* with reference to MRSA isolates from pediatric patients. *Future Sci* OA 2020; 6: FSO464.
- 28. Mitra S, Chayani N, Mohapatra D, Barik MR, Sharma S, Basu S. High prevalence of biofilm-forming MRSA in the conjunctival flora in chronic dacryocystitis. *Semin Ophthalmol* 2019; 34; 74-79.
- Frazee BW, Lynn J, Charlebois ED, Lambert L, Lowery D, Perdreau-Remington F. High prevalence of methicillin-resistant *Staphylococcus aureus* in emergency department skin and soft tissue infections. *Ann Emerg Med* 2005; 45: 311-320.
- Johansson PJ, Gustafsson EB, Ringberg H. High prevalence of MRSA in household contacts. *Scand J Infect Dis* 2007; 39: 764-768.
- Japoni A, Jamalidoust M, Farshad S, Ziyaeyan M, Alborzi A, Japoni S, et al. Characterization of SCCmec types and antibacterial susceptibility patterns of meth-

icillin-resistant *Staphylococcus aureus* in southern Iran. *Jpn J Infect Dis* 2011; 64: 28-33.

- 32. Khoshbayan A, Shariati A, Ghaznavi-Rad E, van Belkum A, Darban-Sarokhalil D. Prevalence and molecular epidemiology of ceftaroline non-susceptible methicillin-resistant *Staphylococcus aureus* isolates, first clinical report from Iran. *Acta Microbiol Immunol Hung* 2020; 67: 228-233.
- 33. Suwantarat N, Rubin M, Bryan L, Tekle T, Boyle MP, Carroll KC, et al. Frequency of small-colony variants and antimicrobial susceptibility of methicillin-resistant *Staphylococcus aureus* in cystic fibrosis patients. *Diagn Microbiol Infect Dis* 2018; 90: 296-299.
- 34. Dibah S, Arzanlou M, Jannati E, Shapouri R. Prevalence and antimicrobial resistance pattern of methicillin resistant *Staphylococcus aureus* (MRSA) strains isolated from clinical specimens in Ardabil, Iran. *Iran J Microbiol* 2014; 6: 163-168.
- Brown PD, Ngeno C. Antimicrobial resistance in clinical isolates of *Staphylococcus aureus* from hospital and community sources in southern Jamaica. *Int J Infect Dis* 2007; 11: 220-225.

- 36. Tsige Y, Tadesse S, G/Eyesus T, Tefera MM, Amsalu A, Menberu MA, Gelaw B. Prevalence of methicillin-resistant *Staphylococcus aureus* and associated risk factors among patients with wound infection at referral hospital, northeast Ethiopia. *J Pathog* 2020; 2020: 3168325.
- 37. Berglund C, Mölling P, Sjöberg L, Söderquist B. Predominance of staphylococcal cassette chromosome mec (SCCmec) type IV among methicillin-resistant *Staphylococcus aureus* (MRSA) in a Swedish county and presence of unknown SCCmec types with Panton-Valentine leukocidin genes. *Clin Microbiol Infect* 2005; 11: 447-456.
- Deurenberg RH, Stobberingh EE. The evolution of Staphylococcus aureus. Infect Genet Evol 2008; 8: 747-763.
- 39. Dhawan B, Rao C, Udo EE, Gadepalli R, Vishnubhatla S, Kapil A. Dissemination of methicillin-resistant *Staphylococcus aureus* SCCmec type IV and SCCmec type V epidemic clones in a tertiary hospital: challenge to infection control. *Epidemiol Infect* 2015; 143: 343-353.