

Community-acquired methicillin-resistant *Staphylococcus aureus* carriage rate and antimicrobial susceptibility in a tertiary center, Iran

Shervin Shokouhi, Ilad Alavi Darazam, Mohammad-Hossein Zamanian

Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background: This study was aimed to determine frequency and antimicrobial susceptibility of Community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) among colonized patients in outpatient status. **Materials and Methods:** A total of 2000 nasal nares specimens were collected and inoculated on mannitol salt agar. MRSA were identified based on mannitol positivity and coagulase test followed by ceftoxitin disc diffusion test. Antimicrobial susceptibility of MRSA isolates was performed by E-test method for vancomycin and doxycycline as well as disc diffusion method for sulfamethoxazole-trimethoprim (SMX-TMP), erythromycin, linezolid, and clindamycin. D-test was performed for detection of inducible resistance to clindamycin. **Results:** Overall, nasal carrier rate of *S. aureus* and CA-MRSA was estimated 22% and 1.25%, respectively. Out of the 440 *S. aureus* isolates, 25 isolates were MRSA. All were susceptible to vancomycin and linezolid, and susceptibility rates to SMX-TMP, erythromycin, levofloxacin, doxycycline, and clindamycin were 68%, 44%, 48%, 40% and 44%, respectively; furthermore, 28.5% of resistant isolates to erythromycin had inducible resistance to clindamycin. **Conclusion:** It seems susceptibility to clindamycin and SMX-TMP, recommended agents for empirical treatment of suspected CA-MRSA, are not promising. Vancomycin and linezolid are effective and reliable antibiotics for the treatment of *S. aureus* infections.

Key words: Antimicrobial susceptibility, Community-acquired methicillin-resistant *Staphylococcus aureus*, nasal carrier

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INTRODUCTION

Staphylococcus spp. (species) are among the first identified human pathogens and *Staphylococcus aureus* is the most important human pathogen in this genus.^[1] They mostly colonize in the nose, perinea, and damaged skins. About 20% and 60% of the population are colonized permanently and intermittently by these bacteria, respectively.^[2] Following the introduction of penicillin in the 1940s, the penicillin-resistant strains were gradually reported in 1945. Therefore, methicillin was introduced in 1959; however, the methicillin-resistant *S. aureus* (MRSA) were identified

soon after its administration in 1961. Vancomycin is a selected antibiotic to treat MRSA infections,^[3] but resistance to vancomycin in MRSA species was also reported in the studies.^[4] It seems that the epidemiology of MRSA is changing in a way that the isolation of MRSA species is not only limited to the hospitalized patients or those with high-risk underlying factors anymore.^[5]

Recently, some cases with MRSA infection and no hospitals or health-care setting associated risk factors were reported; the risk factors which were always observed in association with MRSA infections previously.^[6,7] Since these infections are seemingly acquired from the community, the term "community-acquired" was given to them.

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Address for correspondence: Dr. Shervin Shokouhi, Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti University of Medical Sciences, Velenjak Koodakyar Ave., P.O. Box 1985717443, Tehran, Iran. E-mail: shsh.50@gmail.com

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The risk factors associated with the community-acquired MRSA (CA-MRSA) are not exactly identified. There are some reports on epidemics of CA-MRSA in the communities such as prisoners, military troops, professional athletes, and children going to kindergarten; the reports, which can be useful to identify CA-MRSA associated risk factors.^[4,8-10]

Out of the hospitals, some people carry MRSA, called MRSA carriers or those who colonized with MRSA and can be the reservoir of these microorganisms.^[11] Person-to-person transmission of these bacteria was reported in some studies.^[12] On the other hand, controlling such infections is complicated due to the simultaneous resistance of MRSA to the antibiotics. Naderi *et al.* reported the isolation of *S. aureus* with low sensitivity to vancomycin in Mashhad, Iran.^[13] The rate of antibiotic resistant *S. aureus* and bacteria carriers is highly variable in different studies, depending on the employed identifying methods.

Results of the studies indicated that the global rate of MRSA is increasing annually. For example, in the USA the level of MRSA increased from 23.4% in 1997 to 34.4% in 2002.^[14] Based on the report of center for disease control and prevention, more than 50% of nosocomial infections in patients admitted to the intensive care units caused by MRSA species. In addition to antibiotic therapy, *S. aureus* infection is highly prevalent among hospitalized patients and is associated with severe complications.^[15]

The steady increase of drug-resistant bacteria and associated infections has dragged scientists' attention. Therefore, MRSA is considered as one of the major public health concerns because of its resistance to antibacterial drugs and agents.^[2]

Finally, being aware of CA-MRSA prevalence among the community can affect the hospital infection controlling policies. Following "the search and destroy policy" in some West European countries has significantly decreased the prevalence of hospital-acquired MRSA (HA-MRSA).

Data on prevalence, risk factors, and antibacterial resistance of these bacteria are constantly changing. On the other hand, geographical differences can perfectly affect these factors. The current study aimed to evaluate the prevalence, infection, and antibiotic resistance patterns of MRSA in a considerable sample size of outpatients referred to three teaching hospitals in Tehran during January–December 2015.

MATERIALS AND METHODS

Study design, participants

The current cross-sectional study was conducted on 2000 outpatients referring to three teaching hospitals (Loghman, Imam Hussein and Labbafinejad hospitals located, three

general and multi-speciality hospitals, associated with Shahid Beheshti university of medical sciences) in Tehran during January–December 2015. All outpatients who gradually referred to the hospital were enrolled in the study. People with high risks of HA-MRSA were excluded from the study. The exclusion criteria were injecting drug users, patients undergoing hemodialysis in medical centers, patients with HIV and those who took antibiotics within the last 3 months and history of admission to medical centers during the last year.

Procedures and measuring variables

Samples were obtained from anterior nares by nasal swabs; then, the samples were cultured on mannitol salt agar and incubated at 35°C for 24 h. To isolate *Staphylococcus* spp., yellow colonies were transferred onto blood agar plates and incubated at 35°C for 24 h. Then, samples with positive mannitol test results were retested for coagulase by DNase to separate coagulase positive species. Then, after disc diffusion method was employed to determine the level of resistance to ceftioxin and identify MRSA species. To determine the minimum inhibitory concentration of vancomycin and doxycycline of MRSA species the E-test, and to determine the level of sensitivity of MRSA species to sulfamethoxazole-trimethoprim (SMX-TMP), erythromycin, clindamycin, and linezolid the disc diffusion methods were used. Resistant species were categorized based on instructions of the Clinical and Laboratory Standards Institute (CLSI).^[16]

Statistical analysis

The results for qualitative variables were presented as percentages, and quantitative variables were presented as mean and standard deviation.

RESULTS

Out of the 2000 nasal swab samples obtained from the 2000 patients (44% female, 56% male), 440 (22%) were *S. aureus* carriers, which 25% out of them were MRSA. The prevalence of CA-MRSA among *S. aureus* carriers was 5.68%. The total prevalence of CA-MRSA in the study population was 1.25% [Table 1].

Table 1: Frequency of *Staphylococcus aureus* nasal carrier state including methicillin-resistant *Staphylococcus aureus* and community-acquired methicillin-resistant *Staphylococcus aureus*

Carrier state	n (%)
Carriers	
CA-MRSA	25 (1.25)
MSSA	415 (20.75)
Noncarriers	1560 (78)

CA-MRSA = Community-acquired methicillin-resistant *Staphylococcus aureus*;
MSSA = Methicillin-susceptible *Staphylococcus aureus*

E-test results indicated all CA-MRSA isolates were susceptible to vancomycin.

Results of the current study also showed that 20% of CA-MRSA species were highly resistant to doxycycline. Based on CLSI categories, 40% of the samples had moderate resistance to doxycycline which indicated ineffectiveness of doxycycline to treat and control the infection. According to the results of the current study, 40% of CA-MRSA isolates were sensitive to doxycycline.

Results of the current study showed that 32% of CA-MRSA species were resistant to SMX-TMP (cotrimoxazole), but two-thirds of the isolates (68%) were sensitive to SMX-TMP.

On the other hand, 40% and 12% of CA-MRSA species were completely and moderately resistant to levofloxacin. According to the results, 48% of CA-MRSA isolates were sensitive to levofloxacin. In addition, only 56% of the isolated bacteria were resistant to erythromycin, which indicated low effect of this antibiotic on CA-MRSA.

Other results showed that 56% of the isolates were resistant to clindamycin. The D-test was used to evaluate the level of resistance against erythromycin in clindamycin-sensitive CA-MRSA isolates; positive results were only observed in four isolates (28.5%), which indicated the induction of resistance to clindamycin. The results of D-test showed high sensitivity of CA-MRSA to linezolid [Table 2].

DISCUSSION

The prevalence of *S. aureus* among the population of the current study was 22%. According to the conducted studies, the prevalence of *S. aureus* is quite different worldwide; for example, 1.1% in Saudi Arabia, 0.3% in India, 0.8% in the USA, and 1.3% in Canada. According to the European Antimicrobial Resistance Surveillance Systems, the prevalence of *S. aureus* along a north-south gradient in Europe was 21%, from 1999 to 2003. In other words, the prevalence of MRSA among North European countries was as rare as <1% and among the South European countries was >30%. The prevalence of MRSA in France, Greece, and Italy was >40% and the highest rate was reported in Romania (73%). In the recent years, the prevalence of MRSA increased globally, even in the areas of low endemicity and reached approximately 24% in Europe in 2004.^[17] It seems

that CA-MRSA species predominantly replace MRSA; it is noteworthy that these bacteria frequently colonize 60% of people.^[18]

The rate of colonization significantly decreased in the community through observing hygiene standards and adopting infection control measures; for example, from 21% to 12% in Estonia and from 33% to 28% in France.^[17]

Another similar study was performed in the north of Iran on 1193 healthy students of primary school. Results showed that 16.3% of the students were *S. aureus* carriers, out of which 34.8% were MRSA.^[18] Nasal carriage was similar to our prevalence in the study of Khorvash *et al.* among healthy people in Isfahan, a central city in Iran.^[19]

Results of the current study were inconsistent with those of Shokouhi *et al.* conducted a decade ago in a health center evaluated in the current study with 2.7% prevalence of MRSA; however, comparing the results of both studies shows a higher rate in the current study (22% vs. 14%). Their study also indicated the effect of risk factors such as place of residence, HIV infection, nasal anatomical abnormalities, and using injecting drugs on nasal colonization of CA-MRSA.^[20] The patients with HIV and injecting drug users were excluded from the current study.

Among the nasal carriers, 5.68% (25 subjects) were antibiotic resistant that is equivalent to 13 per 10,000 people (1.25% of the total population); this is lower than the data obtained from the other communities; for example, in Cyprus this rate was 37.5%, however, is similar to new data from healthy children in Iran (6.1%).^[21,22]

Evaluating antibiotic resistance pattern of *S. aureus* showed that vancomycin and linezolid were the most effective antibiotics to control and inhibit CA-MRSA; clindamycin and erythromycin were less effective compared to other assessed antibiotics.

CA-MRSA species usually show lower resistance against different groups of antibiotics, compared to HA-MRSA species. This may result from the size of these bacteria, which reduces their competency to transmit smaller resistance genes such as staphylococcal cassette chromosome.^[23] Considering the prevalence of antibiotic resistant bacteria, substantial changes should be made in experimental administration of antibiotics to control infections of skin

Table 2: Antimicrobial susceptibility pattern and frequency

	Vancomycin	Doxycycline	Cotrimoxazole	Levofloxacin	Erythromycin	Clindamycin	Linezolid
Sensitive %	100	40	68	48	44	44	100
Resistant (intermediate) %	-	40	-	12	-	-	-
Resistant (high) %	0	20	32	40	56	56	0

and soft tissues in patients referring to emergency ward of hospitals and it is necessary to use more efficient antibiotics against CA-MRSA. In this regard, some scientists believe that experimental administration of vancomycin in areas with high prevalence of CA-MRSA is defensible;^[24] it is consistent with the findings of the current study. None of the isolated species in the current study were resistant against linezolid; this finding supports the result of the study by Rahimi *et al.* conducted in the same area.^[25]

The prevalence of resistance to clindamycin, which includes induction of resistance to this antibiotic is so far reported only in CA-MRSA species with lower resistance; of course, the level of resistance among the species varies based on geographical location.^[26] However, some references report the increasing resistance of CA-MRSA species against clindamycin.^[23] Therapeutic failures were reported following the administration of clindamycin to control infections of skin and soft tissues caused by these bacteria; therefore, if clindamycin is a selective antibiotic to control such infections, the isolated species should be evaluated regarding the antibiotic resistance using D-test.^[26] In the study by Shokouhi *et al.*, 45.5% of the isolated CA-MRSA species showed induced resistance against clindamycin; the rate was 56% among the species isolated in the current study. Accordingly, author does not recommend using clindamycin to control infections cause by MRSA in the studied community.

In some studies, high levels of resistance against erythromycin (up to 93%) among the CA-MRSA isolates were reported.^[20-26] The level of resistance against erythromycin among MRSA species isolated in the current study was 50%; hence, using this antibiotic to control infections caused by these bacteria is not recommended.

CONCLUSION

In total, results of the current study showed that the level of *S. aureus* colonization among the population under study is significant and can perfectly affect management and therapeutic programs of the patients. On the other hand, the prevalence of CA-MRSA species among nonhospitalized patients is insignificant; but considerable changes in antimicrobial sensitivity pattern of these bacteria necessitates revising the experimental treatment of these patients. In other words, experimental administration of antibiotics such as clindamycin, cotrimoxazole, erythromycin, levofloxacin, and doxycycline in patients who are at high risk and suspected of infection with MRSA is not suitable and it is recommended to use more effective antibiotics such as vancomycin and linezolid, before obtaining antibiogram-testing results. However, in cases with no

high-risk factors and not suspected of CA-MRSA, the mentioned antibiotics can be useful.

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Conflicts of interest

There are no conflicts of interest.

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