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Original Article

Staphylococcus aureus: resistance pattern and risk factors

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Abstract

Introduction: Methicillin resistant Staphylococcus aureus (MRSA) has emerged as a nosocomial pathogen of major worldwide importance and is an increasingly frequent cause of community-acquired infections. In this study, different risk factors and MRSA resistance pattern were investigated.

Methods: In a 24 months period, all of the patients who were confined to bed in the surgery ward were included in the study. Then they were assessed to find out as if they had MRSA infection when hospitalized and once when they were discharged. Almost 48 h after admission, when patients were discharged, social and medical histories were acquired. Acquired samples were examined.

Results: During the present study of 475 patients, 108 patients (22.8%) had S. aureus. About frequency of antibiotic resistance among collected S. aureus colonies, erythromycin resistance, was the most frequent antibiotic resistance, also resistance to vancomycin was 0.4% that was the least. Only hospitalization duration had statistically significant correlation with antibiotic resistance, also resistance to erythromycin had statistically significant relation with history of surgery and alcohol consumption. Of all 34 MRSA species, 22 (64.7%) samples were resistant to erythromycin, 17 (50.0%) resistant to cefoxitin, 5 (14.7%) resistant to mupirocin, 1 (2.9%) resistant to vancomycin and 1 (2.9%) resistant to linezolid.

Conclusion: The results of the current study show that among hospitalized patients, there is resistance against methicillin. Since based on results of the study there is resistance against oxacillin and erythromycin in most cases, administering appropriate antibiotics have an important role in minimizing the resistance burden among bacterial species.

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Introduction

Nosocomial infections can be defined as those occurring within 48-72 h of hospital admission, 3 days of discharge or 30 days of an operation. Staphylococcus aureus (S. aureus) is a major pathogen responsible for nosocomial and community-acquired infection. Methicillin resistant S. aureus (MRSA), has emerged as a nosocomial pathogen of major worldwide importance and is an increasingly frequent cause of community-acquired infections that cause significant morbidity and mortality.[1] In 1961, there were reports from the United Kingdom of S. aureus isolates, which resisted to methicillin,[2] and MRSA isolates were soon

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recovered from other European countries, and later from Japan, Australia, and the United States.[3]

The synthesis of large numbers of antibiotics over the past three decades has caused complacency about the threat of bacterial resistance. Bacteria have become resistant to antimicrobial agents as a result of chromosomal changes or the exchange of genetic material via plasmids and transposons.[1] Rates of colonization or infection with MRSA vary by geographic location, type of healthcare facility, and the specific population being studied.[4] Resistance to antibiotics is a significant worldwide problem and antibiotic use is being recognized as the key selective force driving this resistance.[5-9] Traditionally, MRSA was identified infrequently from patients in the community, but over the last few years reports have documented increases in community-acquired MRSA, which may suggest a changing in epidemiology.[10-15]

Colonized personnel can serve as a reservoir for the nosocomial spread of MRSA. Most transmission of MRSA from patient to patient is thought to be mediated by transiently colonized healthcare workers, although airborne dispersal and transmission through contacts with contaminated surfaces may also be important. Isolation measures for patients are intended to interrupt such transmission. Active surveillance and timely identification of MRSA colonization of patients is an important infection control activity that helps to prevent nosocomial spread and is cost-effective.[16]

The center for disease control National Nosocomial Infection Surveillance System reported that MRSA in US hospitals increased from 2.4% in 1975 to 289% in 1991, with a higher degree of resistance in intensive care units.[17] More recent data from 1990 through 1997 identified that the MRSA incidence rate increased 260% in hospitals that participated in the International Networks for the Study and Prevention of Emerging Antimicrobial Resistance program. The reasons for the emergence of MRSA are multi factorial and can be attributed to host factors, infection control practice and antimicrobial pressures.[18]

A recent study by Kallen et al. identified consistent associations and dose-effect relationships that support casual relationships between MRSA and antimicrobial drug use.[10] Hill et al. demonstrated that ciprofloxacin and cephalosporins promoted that colonization and ultimately the spread of MRSA in one hospital.[19] In studies where antimicrobial classes are analyzed separately, both cephalosporins and fluoroquinolones are often identified as risk factors for MRSA.[20] Other risk factors for acquiring resistant species of S. aureus are recent outpatient visit, recent nursing home admission, and recent antibiotic exposure. So in this study S. aureus antimicrobial resistance pattern was investigated, also likely risk factors such as smoking, alcohol consumption, procedure type, gender, and hospitalization duration were taken into account.

Methods

In a 24 months period from October 2010 to October 2012, a study was performed in Sina Educational-Medical Centers, Tabriz, Iran). All of the patients were randomly selected from the hospital admissions by RandList (version 1.2, DatInf GmbH, Tübingen, Germany). Then two nasal samples were obtained with swab, one when patient was confined to bed and the other one when the patient was released (48-72 h later), so nosocomial and community-acquired MRSA infections could have been detected. Nasal samples were cultured on MSA media in streaking pattern. Then they were transferred to the laboratory immediately and incubated for 18-24 h at temperature of 33-35 °C. After this incubation period, cultured samples were categorized into 3 groups: 1. culture samples without any bacteria proliferation or with white colonies; 2. cultured samples with distinguished yellow colonies all over the media; 3. cultured samples with yellow colonies on some part of the media.

First and second categories were respectively known as negative and positive samples of S. aureus. Positive samples were stored at temperature of -71 °C. About the third category, coagulase test was performed. Before performing this test yellow colonies

were cultured on blood agar media and incubated for 24 h, then rabbit serum was used to perform coagulase test. In the other stage, a 0.5 McFarland bacterial suspension was prepared from samples that were cultured on blood agar media and incubated for 24 h according to CLSI (Clinical and Laboratory Standards Institute) 2007 prescription.[21]

This bacterial suspension was used to prepare a spreading plate culture on Mueller-Hinton agar. Then oxacillin and cefoxitin antimicrobial disks were put on cultured samples, which were cultured on Mueller-Hinton agar using bacterial suspension. After 18-24 h of incubation, the samples were inspected for antimicrobial resistance.

The reason why oxacillin antimicrobial disks were used instead of methicillin antimicrobial disk was unavailability of methicillin antimicrobial disk on the open market. Also erythromycin, mupirocin, vancomycin, cefoxitin and linezolid antimicrobial disks were used to examine antimicrobial resistance.

When patients were discharged, information about medical history (e.g. diabetes, hypertension, and ischemic heart disease), addiction history, drug history, social history (smoking and alcohol consumption) and duration of hospitalization was acquired with a checklist filled by same single physician. All participants have signed a written consent, and the study protocol was approved by the Ethics Committee of the Tabriz University of Medical Sciences, which was in compliance with Helsinki Declaration.

Statistical analysis was performed by SPSS software package for Windows (version 16, SPSS Inc., Chicago, IL, USA). Quantitative data are presented as mean ± standard deviation (SD) while qualitative data are demonstrated as frequency and percent (%). Linear correlations were evaluated by Pearson's correlation coefficient and linear regression model. $P < 0.050$ was statistically considered significant in all steps.

Results

During the present study of 475 patients, 108 patients (22.8%) had positive S. aureus with mean age of 42.22 ± 17.06. Some of another demographic information and antibiotic history is shown in table 1. Four patients had a history of surgery (3.2%). In aspect of hospitalization duration, 29 patients (23.0%) were hospitalized for 1 day, 38 patients (30.2%) for 2 days, 30 patients (23.8%) for 3 days and 28 patients (23.0%) for 4 and more days. One-hundred patients (80.0%) had used catheter.

Table 1. Some of demographic information and antibiotic history of patients with positive S. aureus

Variable	Item	Frequency (%)
Age (year)	< 30	38 (30.2)
	30-65	74 (58.7)
	> 65	13 (10.3)
Gender	Male	213 (44.8)
	Female	262 (55.2)
Habits	Alcohol consumption	8 (6.4)
	Smoking	25 (20.0)
Drug history	Metronidazole	243 (51.4)
	Ceftriaxone	239 (50.5)
	Cefazolin	140 (29.6)
	Ampicillin	3 (0.6)
	Clindamycin	4 (0.8)
	Erythromycin	14 (3.0)
History of hospitalization		25 (20.0)
Diabetes		12 (9.6)

S. aureus: Staphylococcus aureus

Frequency of antibiotic resistance among collected S. aureus colonies are shown in figure 1; as it is shown in figure 1 erythromycin resistance was the most frequent antibiotic resistance, also resistance to vancomycin was 0.4% that was the least. In this study, 34 MRSA strains were found. The correlation between demographic information and antibiotic resistance is shown in table 2; only hospitalization duration had statistically significant correlation with erythromycin (P = 0.038), linezolid (P = 0.023) and cefoxitin resistance (P = 0.002), also resistance to oxacillin had statistically significant relation with age and diabetes (P = 0.041 and 0.037 respectively).

Frequency of different surgical procedures is shown in figure 2; appendectomy, cholecystectomy and gallstone removal were most common among other procedures. Examples for others category consists of hydatid cyst removal, colectomy, nephrectomy. Of all 34 MRSA species, 22 samples (64.7%) were resistant to Erythromycin; 17 (50.0%) resistant to cefoxitin, 5 (14.7%) resistant to mupirocin, 1 (2.9%) resistant to vancomycin and 1 (2.9%) resistant to linezolid. Of all medical histories, metronidazole consumption had a statistically significant correlation with resistance to cefoxitin (P = 0.046); correlation between medical history and antimicrobial resistance are shown in table 3.

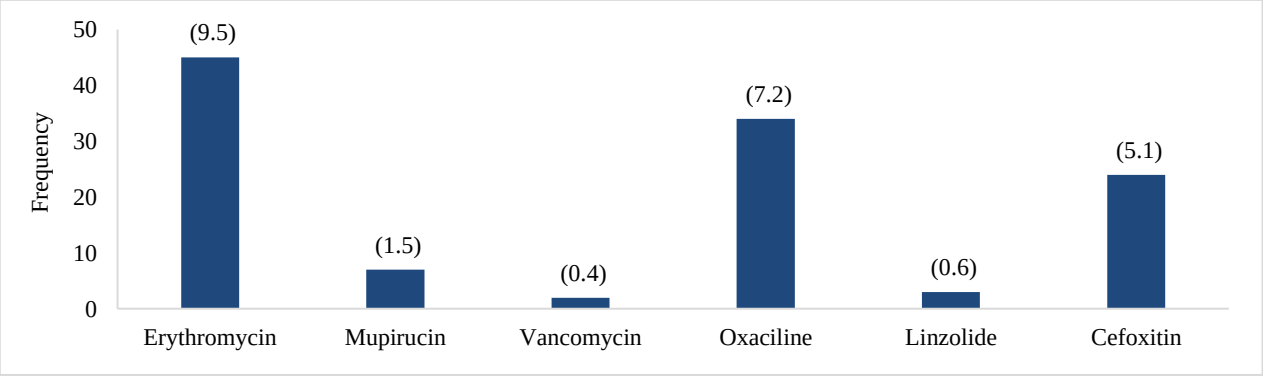

Figure 1. Frequency of resistant Staphylococcus aureus species (%)

Table 2. Correlation between demographic information and antibiotic resistance

Antibiotic variable	Erythromycin	Mupirocin	Vancomycin	Oxacillin	Linezolid	Cefoxitin
Age	0.327	0.314	0.821	0.041	0.838	0.204
Gender	0.540	0.120	0.870	0.400	0.180	0.560
Smoking	0.117	0.490	0.796	0.937	0.725	0.946
Alcohol consumption	0.256	0.522	0.536	0.498	0.533	0.465
History of hospitalization	0.153	0.348	0.562	0.149	0.512	0.341
History of surgery	0.411	0.538	0.549	0.498	0.544	0.516
hospitalization duration	0.038	0.599	0.060	0.063	0.023	0.002
Diabetes	0.318	0.569	0.517	0.037	0.569	0.583

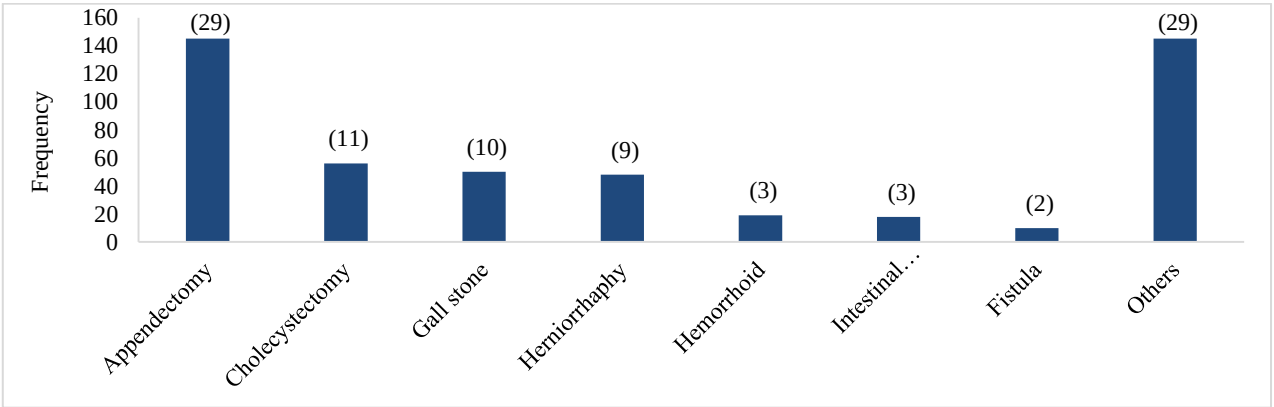

Figure 2. Frequency of different surgical procedures among hospitalized patients (%)

Table 3. Correlation between medical history and antimicrobial resistance among patients

Resistance history	Erythromycin	Mupirocin	Vancomycin	Oxacillin	Linezolid	Cefoxitin
Metronidazole	0.114	0.127	0.082	0.157	0.166	0.046
Ceftriaxone	0.583	0.716	0.734	0.532	0.654	0.174
Cefazolin	0.578	0.874	0.751	0.516	0.885	0.412
Ampicillin	0.640	0.640	0.640	0.640	0.640	0.640
Clindamycin	0.670	0.957	0.984	0.299	0.979	0.849
Erythromycin	0.301	0.709	0.733	0.182	0.728	0.078

Discussion

The results of the current study showed that the prevalence of MRSA is 22.8 % among patients hospitalized in surgery units in Tabriz. The most resistance of S. aureus against investigated antibiotics was resistance against oxacillin and erythromycin.

Prevalence of resistance against methicillin in this study was calculated 7.2%, and this percent is less than expected amount of 40.0% for society and 50-80%.[22] Results of other conducted studies in other parts of Iran and also other countries also show a higher amount of resistance than that of the current study.[23-25] However the results of some other studies show a lower amount of resistance than that of this study.[26,27] For example, the study of Turnidge and Bell in Australia showed prevalence rate of 24.0%.[28] One of the possible reasons for low resistance rate in current study could be investigated due to the method and resource of studying resistance and infection since in this study only nasal samples were taken while in some other studies samples were also taken from various other sources such as blood and urine.

One other possible reason for low prevalence of resistance in current study could be due to higher care of hospitals especially investigated hospital of this study about the issue of nosocomial infections as a result of implementing "Safety Friendly Hospitals" program in which this hospital had been selected as country pilot unit. While resistance amount of this study was lower than that of some studies, but this amount (22.8%) was also a relatively high amount and considering effects, costs and other negative consequences of these infections, the need for developing scientific and effective programs from research centers with coordination of National Committee of Antibiotic Resistance and other authorized centers and organizations for developing a united national system to prescribe and use of antibiotics and to control antibiotic resistances is felt more.

In present study, resistance against the oxacillin (about 7.2%) and erythromycin (about 9.5%) had the highest resistance amount. In this study, background disease (diabetes) had no significant statistical relation with prevalence of resistance. This result was in accordance with the results of the study by Khurram et al.[29] in Pakistan. However, the results of conducted studies in Brazil[30] and America[31] have shown a significant relationship between having background disease and resistance against methicillin.

Based on the results of current study hospitalization period had a significant relationship with antibiotic resistance against cefoxitin. It is in accordance with results of studies conducted in Australia[32] and France.[33] Therefore, we should try to decrease hospitalization period by improving service qualities and provided cares to patients and other effective strategies so that beside decrease in hospital costs and costs imposed to patients and other therapeutic and social aspects, it would be possible to decrease antibiotic resistances and its side effects.

As the main antibiotic therapy for resistant strains of S. aureus (especially MRSA) is vancomycin, always finding strains resistant to vancomycin is a site of concern. In present study, 2 vancomycin resistant strains were found; also other studies have talked about vancomycin resistant strains as a great point of concern.[34-36]

In the present study, prevalence of MRSA was 7.2%. In a study in the Netherlands, less than 1.0% of clinical isolates of S. aureus are MRSA; this low rate was contributed to A

national search and destroy policy prevents MRSA from becoming endemic.[27] In another systematic review about MRSA prevalence in European healthcare settings, it was declared that prevalence rates varied over a wide range, from < 1.0 to > 20.0%. But the overall percentage of MRSA among S. aureus isolates ranged between 5.0 and 54.0%. The screening policy differed with respect to time points (on admission or during the hospital stay), selection criteria (all admissions or patients at high risk of MRSA) and anatomical sampling sites.[37]

One of the weak points of current study was taking only nasal samples from hospitalized patients and it was better to take samples from other possible infected sources such as urine and blood and also from other patients in other wards.

Conclusion

The results of the current study show that among hospitalized patients, there is resistance against methicillin. This subject convinces us to consider guidelines and worldwide standards on the field of infection control especially about methicillin. Also, this issue reminds us the importance and necessity of rational prescription of antibiotics and organizing their prescription to control and decrease colonization rate of MRSA in hospitals. Since based on results of the study there is resistance against oxacillin and erythromycin in most cases, paying more attention to these cases is necessary.

Conflict of Interests

Authors have no conflict of interest.

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