



Investigating Colonization of *Staphylococcus aureus* among Patients Admitted to the Infectious Diseases Ward of Imam Hospital in Mashhad

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ABSTRACT

Introduction: *Staphylococcus aureus* colonization has been recognized as one of the most important risk factors for subsequent infections with this microorganism. In this study, we intended to identify all patients who were MRSA-positive upon admission and compare the prevalence of MRSA colonization on different days of study admitted in Imam Reza hospital in Mashhad, Iran.

Methods: This cross-sectional study was done on 600 admitted patients in Infectious disease ward. Samples of patients were drawn from patients' nares (and if they were culture negative, re-cultures were done on days 3, 7 and finally on discharge time. After identification of the isolates, their susceptibility to methicillin was evaluated. Before we collect nasal swabs, patients filled out a survey questionnaire.

Results: *S. aureus* colonization early after hospitalization in infectious ward was observed in 39.8% (n=239) of patients, of which 59% (n=141) were resistant to methicillin. On the third day of admission, *S. aureus* new colonization rate was 15.8% (n=57), of which 87.7% (n=50) were methicillin resistant. On the seventh day, *S. aureus* were found in 13% (n=32) patients with 90.6% (n=29) were methicillin-resistant. Upon discharge, 8.2% (n=13) patients were *S. aureus* positive and 92.3% (n=12) were resistant to methicillin.

Conclusion: Most of the carriers had the methicillin resistant strains of bacteria at the time of admission, and the number of colonized patients with resistant bacteria increased in time. The most common risk factors in methicillin-resistant *S. aureus* carriers were taking antibiotic, history of prior hospitalization and being an intravenous (IV) drug abuser.

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Introduction

Staphylococcus aureus (*S. aureus*) is a causative agent of many dangerous bacterial infections. It is necessary to be aware of the rate of *S. aureus* colonization, since emerging bacterial infections have higher prevalence in individuals with *S. aureus* colonization. Although *S. aureus* can colonize many sites of human body such as skin, perineum, mouth and intestines, the most common colonization site for *S. aureus* is the anterior nasopharynx. Thus, obtaining a culture from these sites is a common way to distinguish the colonization rate. The colonization rate varies among populations; it was reported between 20-25% in our country (1-5). Nearly 20% of healthy individuals are persistent nasal carriers of *S. aureus*, 30% are intermittent carriers and 50% are not carriers at all. Persistent carriage rate (compared to adolescents and adults) is higher in neonates (approximately 45% in the first 8 weeks after birth), but as time passes it reduces and transitions to intermittent or non-carrier type. The carriage pattern of this bacterium changes in most of adolescents (6, 7). Individuals with Type I diabetes mellitus, dialysis patients, intravenous (IV) drug abusers, patients afflicted with recurrent staphylococcus and HIV infections and those having repeated injections for allergy are more likely to carry this bacterium (8, 9). Colonized patients have higher risk of *S. aureus* infection during and after hospitalization. On the other hand, they act as a causative source of colonization for other individuals to whom they have close contact, especially physicians and nurses, who spread the bacteria to the other patients which colonized in patients without initial colonization at the time of admission. Methicillin resistant *Staphylococcus aureus* (MRSA) strains were initially described in 1961 and emerged over the past few decades as one of the most important nosocomial pathogens. As a major problem with treatment, methicillin resistance has made the eradication of staphylococcal infections more difficult (9, 10).

This microorganism can colonize people admitted to hospitals, and to a lesser extent people out of hospitals. In recent years, the prevalence of community-acquired MRSA has increased in certain populations in the community, resulting in more admissions to hospitals and increasing the number of patients who are MRSA-positive at the time of admission and can then spread the organism to other patients in the hospital (11). Given that, our objective was to identify all patients who were MRSA-positive upon admission and compare the prevalence of MRSA colonization on different days of study (at the time of admission, third day, seventh day and upon discharge).

Material and method

In this cross-sectional study, the study population included patients admitted directly to the infectious disease ward within year 2008. Samples were drawn from each patient within 20 hours of admission. Samples were collected from both anterior nares of all 600 patients upon admission by sterile broth-soaked swab and was inserted into anterior part of each nostril in turn, to a depth of approximately 1 cm, and rotated five times to detect MRSA colonization (12). At the time of nasal swab collection, patients filled out a survey questionnaire and patients signed the consent form. A nurse was available to clarify questions as needed. The samples were immediately cultured in blood agar and mannitol salt agar media (Merck), separately. Petri dishes were then incubated for 24-48 hours in 35°C. The isolates were identified as *S. aureus* based on morphology, Gram stain, catalase test, and coagulase test and mannitol salt agar fermentation. Then, methicillin susceptibility results were interpreted based on inhibitory zone of oxacillin disks (Mast Company, UK) according to Clinical and Laboratory Standards Institute (CLSI) guidelines (13). In case of negative-culture result, another sample was obtained from the

patient on the third day. If the third-day culture was also negative, seventh-day culture was done and if it was negative, the last culture was done upon discharge. If the culture of a patient became positive in each stage of hospitalization, no further culture was done. Using this method, those without colonization in the beginning of hospitalization were monitored for colonization in the hospital. We recorded and documented chief complaint, age, gender and other demographic information of the patients. Risk factors of MRSA colonization including type I diabetes mellitus, peritoneal or blood dialysis, drug injection, taking antibiotics within the past three months, history of surgery or hospitalization within the last year, history of admission to the intensive care unit (ICU), malignancies and residing in nursing homes has been assessed and recorded as well. Then, risk factors were encoded and recorded for each patient (if the patient had more than 3 risk factors, we only recorded up to three risk factors). The results were evaluated using SPSS software.

Ethical considerations

Informed oral consent was obtained from all patients before specimen collection. The ethical committee of Mashhad University of Medical Sciences approved the study. Ethical issues including privacy of personal data were considered during all steps of the research.

Result

In this study, began in March 2008 and continued for one year, 600 hospitalized patients were evaluated. Average age of patients admitted to infectious disease ward was 49 ± 2.12 years. Minimum and maximum ages were 14 and 92, respectively. 59% of patients were male and 41% were female. Among 600 hospitalized patients, 239 (39.8%) patients had positive nasal culture and 361 (60.2%) were culture-negative for *S. aureus* at the time of admission. On the third day, 57 patients (15.8%) had positive and 304 patients (84.2%) had negative culture for *S. aureus*. Nasal cultures of 32 patients (13%) were positive and 214 patients (87%) were negative on the seventh day for *S. aureus*.

Table1. Frequency distribution of culture result and MRSA for admission day

Results of culture Admission time	Positive (N(%))		Negative (N(%))	Total (N(%))
	Total	MRSA		
Upon admission	239 (39.8)	141 (59)	361 (60.2)	600 (100)
3rd day of admission	57 (15.8)	50 (87.7)	304 (84.2)	361 (100)
7th day of admission	32 (13)	29 (90.6)	214 (87)	246 (100)
Discharge day	13 (8.2)	12 (92.3)	145 (90.8)	158 (100)
Total	341 (57)	232 (68)	259 (43)	600 (100)

Finally on the discharge day, 13 patients (8.2%) had positive and 145 patients (90.8%) had negative culture for *S. aureus* (table 1). We found that, patients who developed MRSA colonization were admitted for a longer period. Among patients having *S. aureus* nasal colonization at the time of admission, 141 (59%) had MRSA and 98 (41%) were colonized with methicillin-sensitive *S. aureus* (MSSA). On the third day this proportion reached to 87.7% (n=50) for MRSA and 12.3% (n=7) for MSSA. On the seventh day, 29 (90.6%) and 3 (9.4%) of patients had positive culture for MRSA and MSSA, respectively. On the day of discharge, 12 patients (92.3%) were colonized with MRSA and one patient (7.7%) was colonized with MSSA (table 1). Colonization extent with MRSA in hospitalized patients had an increasing trend over time. During the first day of admission, 59% of patients, who were colonized by *S. aureus*, were MRSA positive. On the third day, this percentage increased to 87.7 and on the seventh day to 90.6. Finally, on the day of discharge, 92.3% of patients were colonized with MRSA. In this study, frequency of nine risk factors related to *S. aureus* colonization (as mentioned above) was evaluated. Totally, 316 patients (52.7%) admitted to infectious diseases ward had at least one risk factor and 284 (47.3%) did not have any risk factors. Our results showed 107 (37.7%) out of 284 patients without a risk factor had *S. aureus* colonization in the beginning of admission, forty seven of which (44%) were MSSA and 60 (56%) were MRSA. In this study, 316 patients had risk factors at the time of hospitalization, from which 185 (59%) had no colonization and 131 (41%) were colonized by *S. aureus*. Methicillin sensitivity test showed that 51 (39%) of these patients were susceptible to methicillin and 80 (61%) were methicillin-resistant. Out of 239 patients who were colonized with *S. aureus* at the beginning of admission, 108 patients (45%) had no risk factor and 131 patients (55%) had risk factors. This study showed that history of hospitalization, taking antibiotics and injecting drugs were the most important risk factors for colonization of MRSA. Patients

admitted to infectious diseases ward had sometimes more than one single risk factor. The percentage of patients who had one, two and three risk factors was 29.3, 17.2 and 6.2, respectively. In general, 60.2% of patients admitted during the study time had no *S. aureus* colonization, while 23.5% of them were colonized with MRSA and 16.3% with MSSA.

Discussion

Frequency of MRSA colonization at the time of admission is of epidemiological importance because patients admitted with either MRSA infection or colonization can transmit the bacteria to other people in the hospital (11). In this research, the prevalence of new colonization during hospitalization was studied. Also, in each patient, presence of *S. aureus* colonization risk factors was sought and recorded. High prevalence of risk factors in individuals at the time of admission was associated with high probability of MRSA colonization. The criteria are reminders to perform patient isolation and decolonization. They are also important in choosing a suitable antibiotic at the time of infection in such an individual against MRSA. In a study in Lebanon, the percentage of nasal carriers of this bacterium was reported 38.4% most of which were children aged 6-10 years old (14). Haley and coworkers showed that out of 401 patients, 41 (10%) had positive cultures for MRSA at the time of admission (11). Wertheim *et al* found 24% of the patients to be nasal carriers of *S. aureus* at the time of admission, but only three (0.03%) patients were MRSA carriers (15). In a study done by Olsen *et al*, the prevalence of *S. aureus* nasal carriage was 26.2% and 26% in health care workers and non-health care workers, respectively. They also reported working in health care services and residing with children as potential risk factors for nasal carriage of *S. aureus* (16). According to the study done by Hidron *et al*, 53 (7.3%) of 726 patients had a positive culture of nares for MRSA, and 119 (16.4%) had a positive culture for MSSA.

Risk factors with an increased risk of MRSA colonization included hospitalization during the last 12 months, presence of skin or soft-tissue infection on admission and taking antibiotics within the last 3 months (17). In this study, the prevalence of MRSA colonization on admission in our study population was 23.5% (141 out of 600 patient), which is higher than the findings of similar studies (11, 18, 19). On the other hand, our study population was larger than many similar studies (11, 18). In our study, out of 600 study patients, 239 were initially colonized with *S. aureus*. 141 (59%) were colonized with MRSA, and 98 (41%) were colonized with MSSA. Davis *et al* reported 163 out of 758 patients (21%) to be initially colonized with *S. aureus*, of which 26 (15.9%) were colonized with MRSA, and 137 (84.1%) with MSSA (18). We also found that, patients who subsequently developed MRSA colonization were admitted for a longer period. This is similar to what Davis *et al* reported in their study (18). Identifying MRSA colonization or infection on admission has become an important challenge in reducing subsequent nosocomial transmission (11). In a study conducted in an American hospital in 2003, factors independently related to MRSA colonization were reported as follows: history of hospitalization in the last year, presence of skin or soft tissue infection at the time of hospitalization, taking antibiotics within the last three months and HIV status of the patient. Higher incidence of MRSA colonization in this study in comparison with former reports (5.3-13%) was attributed to demographic and predisposing factors, history of multiple hospitalizations and chronological changes in MRSA colonization trend (19). Furuno and colleagues performed nasal culture for patients newly admitted to NICU, to evaluate carriage status of *S. aureus* indicating 7.2% colonization rate. They had risk factors such as hospitalization within the last year and taking antibiotics before hospitalization (20). Jernigan *et al* isolated *S. aureus* from 205 patients (21%).

Further investigations revealed that 179 (18.4%) of patients had MSSA and 26 (2.7%) had MRSA. All 26 MRSA-colonized patients had been admitted to a healthcare facility in the preceding year, had at least one chronic illness, or both (21). In a study done in a surgical unit of a hospital in India, out of 100 health care workers from 5 surgery wards, 13 (13%) were carriers of *S. aureus*, two of whom (15.4%) were MRSA carriers. The authors recommended performing periodic screening for all health care workers in order to reduce the rate of carriage (22). Santos *et al* reported 16 adult patients of a total 297 that had been colonized with MRSA at the time of admission. Hospitalization in the last year and more than 60 years of age were factors associated with colonization in adults (23). In another study done in India which investigated the rate of *S. aureus* carriage in children aged up to 5 years which turned out to be 6.3%, 16.3% of which were MRSA. The risk factors associated with *S. aureus* carriage were taking part in school and living in large families (24). In our study, the rate of colonization with *S. aureus* in the time of admission was 39.8%, of which 16.3% was by MSSA and 23.5% by MRSA. 64% of our subjects reported a history of hospitalization for at least one time in the previous year, which was associated with colonization at the time of admission. In similar studies, there has been a range of colonization from 14.6% to 24.4%, with methicillin resistant cases from 0.03% to 12.9%. The mentioned studies have been performed in different wards such as ICU, midwifery, orthopedics, internal medicine and so on and in many of them colonization risk factors have also been evaluated. By contrast, colonization ratio upon admission of patients in our study is nearly as twice as the other studies. One reason for these results is the high proportion of patients with colonization risk factors, consisting 52.7% of all admitted patients. Each of these patients had one to three risk factors. Considering this high colonization rate upon admission, especially with MRSA, and reminding the fact that these

patients are subject to a high risk of subsequent infections with the same colonized bacterium, it seems necessary for infectious wards to have a screening program at the time of admission, for high risk patients followed by a decolonization program (or strategy). In the present study, 15.8%, 13% and 8.2% of patients without initial colonization were colonized by *S. aureus* on the third day, seventh day and upon discharge, respectively. It seems that antibiotic administration for most of the patients without initial colonization may have reduced the colonization rate. Nasal colonization of the patients in the hospital is probably by MRSA, regarding the high colonization rate by the bacterium in third and seventh days of admission and also in discharge day. According to the latest CLSI guideline, methicillin susceptibility is determined by cefoxitin disk diffusion test, and all *Staphylococcus aureus* isolates with cefoxitin disk inhibition zones of 21mm or less in diameter should be considered as MRSA. Given that, using oxacillin disk diffusion method in this study is one of our limitations. This limitation was due to unavailability of cefoxitin disks and using old guidelines in Mashhad hospital laboratories, at the time we performed our study (13, 25). In conclusion, admitted patients become colonized with nosocomial pathogens such as *Staphylococcus aureus* as time passes. Furthermore, longer time of hospitalization and having mentioned risk factors are associated with higher probability for bacteria to become resistant against antibiotics. Thus, less antibiotic prescription and reducing the time of hospitalization if possible are recommended.

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Conflict of interest

None declared conflicts of interest.

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