

# Colonization With Methicillin-Resistant *Staphylococcus aureus* Upon Intensive Care Unit Admission: Incidence and Risk Factors

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## Abstract

**Background:** Since earlier identification of methicillin-resistant *Staphylococcus aureus* (MRSA)-colonized patients could be helpful for reducing the overall frequency of *S. aureus* infections, the investigation of persons colonized with MRSA is considered to be a key component of MRSA infection prevention programs, particularly among ICU patients.

**Objectives:** The aim of the present study was to evaluate the prevalence of nasal and extra-nasal carriers of MRSA and risk factors associated with MRSA colonization among adult patients admitted to the ICU.

**Methods:** In a cross-sectional study, 164 adult patients who were admitted to the ICU of a teaching hospital were screened for nasal and extra-nasal carriage of MRSA. In addition, the ICU-hospitalized patients were evaluated for MRSA acquisition during their ICU stay.

**Results:** Out of the 164 patients admitted to the ICU, 12 (7.3%) patients were methicillin-susceptible *Staphylococcus aureus* (MSSA) carriers, and 12 (7.3%) patients carried MRSA. Four (16.6%) patients were colonized at single or multiple extra-nasal sites based on negative nares screening. Of the 15 remaining patients hospitalized at the ICU, one (6.7%) patient acquired MRSA. The patients colonized with MRSA had more advanced ages ( $P = 0.008$ ), longer hospital stays before being transferred to the ICU ( $P > 0.001$ ), more underlying diseases with chronic obstructive pulmonary disease (COPD) ( $P = 0.028$ ), and had undergone surgery ( $P = 0.003$ ). Patients transferred from the surgical wards to the ICU were found to have significantly higher carriage rates of MRSA ( $P = 0.041$ ).

**Conclusions:** The prevalence of MRSA colonization upon ICU admission at our hospital was relatively high, and routine MRSA screening is suggested, especially for patients who have certain risk factors. In addition, extra-nasal MRSA screenings upon ICU admission will help in the early detection of MRSA.

**Keywords:** Intensive Care Units, Methicillin-Resistant *Staphylococcus aureus*, Patient Admission

## 1. Background

*Staphylococcus aureus* is one of the most important pathogens involved in serious infections in humans. Before the emersion of antibiotics, *S. aureus* was responsible for more than 80% of deaths in infected patients (1). In the mid-1940s, the prognosis of patients improved with the introduction of penicillin. However, the continued use of this type of antibiotic led to the development of strains resistant to penicillin due to their ability to synthesize beta-lactamase (2). Methicillin synthesized in 1959, but in 1961, *S. aureus* isolates had acquired resistance to methicillin and the first methicillin-resistant *S. aureus* (MRSA) case was reported (3).

*S. aureus* colonizes various sites of the human body. The primary *S. aureus*-colonization regions are the anterior nares of the nose, skin, perineum, gastrointestinal

tract, vagina, and axilla (1, 4). The relationship between *S. aureus* nasal carriage and staphylococcal infections was first reported by Danbolt in 1931. Colonization with *S. aureus* (methicillin-susceptible *S. aureus* (MSSA) and MRSA) is a major risk factor for developing nosocomial infections among patients admitted to intensive care units (ICUs). Furthermore, MRSA infection is associated with higher mortality rates, expensive care, and longer hospital stays (4). In different studies, MRSA colonization varied from 3% to 47% of patients upon ICU admission (5-10), and 5% to 12% of patients were colonized with MRSA during hospitalization (11). The risk of becoming colonized during a stay at an ICU is dependent on a number of variables, such as age, previous hospitalization, hospitalization at the ICU, chronic medical illness, prolonged antibiotic usage, presence of any wound, and invasive indwelling devices (12, 13).

Since the earlier identification of high-risk patients (MRSA-colonized patients) could be helpful for reducing the overall frequency of *S. aureus* infections, MRSA nares screening is considered to be a key component in MRSA infection prevention programs in hospitals, particularly among ICU patients (14). Furthermore, due to the fact that *S. aureus* colonizes different parts of the body, the additional investigation of persons colonized with MRSA at extra-nasal body sites may be important for finding the initially-unrecognized reservoirs of MRSA in hospitals.

## 2. Objectives

The aim of the present study was to evaluate the prevalence of nasal and extra-nasal carriage of MSSA and MRSA and the risk factors associated with MRSA colonization among adult patients admitted to the ICU. In addition, the rate of MRSA acquisition during the ICU stay was also determined.

## 3. Methods

### 3.1. Study Environment and Population

This cross-sectional study was conducted at the general ICU of Alzahra hospital, a teaching hospital with a capacity of 766 beds located in northern Isfahan, Iran. The study was approved by the Isfahan University of Medical Sciences ethics committee (research project number: 287102). The adult patients hospitalized at the ICU for more than 24 hours between January and September of 2012 were included in the study. During this time, the number of the hospitalized patients was 720. However, only 164 of the patients were hospitalized for more than 24 hours and evaluated for MRSA colonization. Only the first ICU admission during the same hospital stay was included in the analysis. For each patient, the following parameters were determined as risk factors associated with colonization: demographics, date of hospitalization, date of ICU hospitalization, underlying diseases, antibiotic use during this hospitalization, systemic corticosteroid use during this hospitalization, central venous catheterization, mechanical ventilation, nasogastric feeding, tracheostomy, decubitus ulcer, and the previous ward that patient was transferred from to the ICU. Colonization was confirmed if one or more swab samples were positive for MRSA upon admission. If patients remained hospitalized at the ICU for more than one week, then *S. aureus* surveillance swab specimens were collected each week on the same day. Patients who had negative test results for *S. aureus* upon admission were considered at-risk patients, and were classified as ICU-acquired if the first positive sample *S. aureus* was obtained at least one week after ICU admission.

### 3.2. Sample Collection and Laboratory Methods

Swab specimens were collected separately from the anterior nares, axillary, and perinea of each patient. Nasal swabs were obtained by inserting a cotton swab 2 cm into one naris and rotating the swab 360°; the procedure was repeated in the second naris. Axillary and perineal swabs were collected by moistening each swab with sterile normal saline. Swabs were then placed into the Amies transport medium, and delivered to the microbiology laboratory within one hour.

Swab specimens were inoculated onto blood agar plates (Merck, Germany) with 5% sheep blood. The plates were incubated at 35°C and examined for growth after 24 - 48 hours. Strains that grew on the plates were confirmed as *S. aureus* by using the following tests: gram staining, 3% catalase, coagulase, deoxyribonuclease (DNase) testing, and growth on a Mannitol-salt-agar medium. Confirmed *S. aureus* isolates were sub-cultured on Muller-Hinton agar (Merck, Germany) containing 6.0 µg/mL of oxacillin (Mast, UK) to determine whether they had methicillin resistance. Plates were incubated at 35°C for 18 - 24 hours and examined for evidence of growth. Strains showing distinct growth were considered to be methicillin resistant.

### 3.3. Statistical Analysis

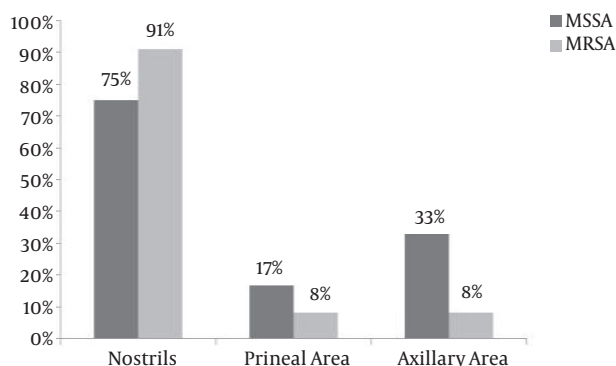
Statistical analysis was performed using SPSS v. 19.0. Appropriate  $\chi^2$ -tests and Yates's correction for continuity were used for the analysis. Odds ratios (OR) and 95% confidence intervals (CIs) were also calculated. A two-sample t-test was used to compare means between two continuous variables. The Mann-Whitney U test was used to compare medians between two non-parametric continuous variables. Statistical significance was set at  $P \leq 0.05$ .

## 4. Results

During the study period, 164 patients were screened for *S. aureus* carriage. In total, 94 (57.3%) of the patients were male, and the mean age of the patients was  $51.87 \pm 20.656$  years (range: 18 - 90). The hospital length of stay (HLS) before transfer to the ICU was calculated for each patient. The mean HLS for all patients was  $5.27 \pm 11.061$  days (range: 0 - 63). In this study, 67 (40.9%) patients were transferred to the ICU from surgical wards, 58 (35.4%) from the emergency room, and 39 (23.8%) from other wards.

Out of the 164 patients admitted to the ICU, 24 (14.6%) patients were *S. aureus* carriers. Out of this number, 12 (50%) carried MSSA, and 12 (50%) carried MRSA (7.3% of all patients for both MSSA and MRSA). Referring to the site of colonization, MRSA was detected more than MSSA in various areas (Figure 1). We evaluated the patients for the presence of single or multiple sites of colonization, and found

that four (16.6%) patients were colonized at multiple sites. Also, we found that four (16.6%) patients were colonized at single or multiple extra-nasal sites with negative nares screening (one (4.2%) MRSA and three (12.5%) MSSA).



**Figure 1.** Distribution of the 24 Colonized Patients with MSSA and MRSA According to the Sites of Colonization

Of the 140 patients who were not colonized with *S. aureus* upon admission, 15 patients remained hospitalized in the ICU long enough to have their potential acquisition assessed with at least one follow-up swab sample. Of these at-risk patients, one (6.7%) patient acquired MRSA during a one-week ICU stay.

The demographics and clinical characteristics of the 24 colonized patients are shown in Table 1. At the time of sampling, the patients colonized with MRSA had more advanced ages, a longer HLS before transfer to the ICU, more underlying diseases with chronic obstructive pulmonary disease (COPD), and had undergone surgery (Table 1).

The detailed distribution of the carriage rates of MRSA and MSSA in various wards from which patients were transported to the ICU are shown in Table 2. Patients who were transferred from the surgical wards to the ICU had significantly higher carriage rates of MRSA (66.7% vs. 25%; odds ratio (OR): 0.167; 95% confidence interval (CI): 0.028 - 0.983;  $P = 0.041$ ), while the patients who were transferred from the emergency room to the ICU had significantly higher carriage rates of MSSA (58.3% vs. 16.7%; OR: 7.00; 95% CI: 1.04 - 46.94;  $P = 0.035$ ).

## 5. Discussion

Active screening of patients for MRSA carriage is becoming routine in many parts of the world (14, 15). Recognition of MRSA colonization may potentially be beneficial for preventing the spread of MRSA among hospitalized patients (16). Our data showed that 14.6% patients were *S. aureus* carriers, and 7.3% patients were colonized with MRSA.

The MRSA prevalence at our ICU was lower than those rates previously reported in other studies (usually more than 10%) (5, 7, 17, 18), yet 50% of the overall isolated *S. aureus* were MRSA. This may reflect the higher rate of MRSA amongst hospital-acquired *S. aureus* infections at our hospital.

The rate of colonization varies in different parts of the world. Also, based on the site of sampling and MRSA detection methods, the percentage of MRSA colonization among the population also varies. In most of the studies, screening for MRSA has been performed at the nares alone; nevertheless, McKinnell and colleagues suggested that extra-nasal testing would increase the number of patients identified as MRSA carriers (14). In our study, we found 4.2% of MRSA colonization cases through extra-nasal testing. Extra-nasal colonization with MRSA can increase the contamination of healthcare personnel's hands and medical equipment. However, the transmissibility of MRSA from extra-nasal body sites compared to nasal transmission was not sufficiently investigated. Understanding the effects of extra-nasal body site MRSA colonization on the causes of infection among ICU patients may reveal effective targets for MRSA screening, and should be considered in future studies.

In our study of the 15 at-risk patients, one (6.8%) became colonized with MRSA. Bloemendaal et al. reported 4% of at-risk patients being colonized during their ICU stays (12). This is a slightly lower rate than our findings. They also showed that colonization pressure, the number of beds per nurse, and the treatment of all patients in private rooms correlated with the number of acquisition cases at the ICU. Unfortunately, our study had a short period of inclusion, and as a result, a low number of acquisition cases. We failed to find a correlation between the rate of acquisition and the efficacy of the intervention measure. However, the patient who became colonized with MRSA in our study had undergone surgery and gastrostomy, and both of these factors could influence the acquisition rate at an ICU (12, 13).

According to Kavanagh et al., "We live in harmony with commensal bacteria and are harmed by pathogenic bacteria. The importance of the types of bacteria residing on and in the body cannot be overstated. The effects of antimicrobial agents on the microbiome is not only that bacteria may develop antimicrobial resistance, but also that a selective advantage may be produced for other bacteria, sometimes even more virulent, that then take the place of the eradicated pathogen" (19). As an example, MSSA is one type of commensal bacteria that can be replaced by MRSA, and this replacement has serious consequences.

In the present study, the mean age of the MRSA-colonized patients was significantly higher than that of the MSSA-colonized patients ( $P = 0.008$ ). Honda et al. also

**Table 1.** Comparison of Demographics and Clinical Characteristics Between Subjects Colonized with MRSA and MSSA

Variables	No.(%) of Subjects			OR (95% CI)	P Value
	MRSA	MSSA	Total		
Male gender	9 (75)	6 (50)	15 (62.5)	1.28 (0.52 - 3.13)	0.206
Age, y, mean $\pm$ SD <sup>a</sup>	59.91 $\pm$ 20.66	38.41 $\pm$ 14.80	49.16 $\pm$ 20.72	-	0.008 < 0.05
Median of hospital sta, d, quartiles <sup>b</sup>	10 (3.5 - 32)	1 (0 - 1)	2.5 (1 - 12.5)	-	< 0.001
COPD	4 (33.3)	0 (0)	4 (16.6)	1.55 (0.47-5.11)	0.028 < 0.05
Diabetes mellitus	3 (25)	2 (16.7)	5 (20.8)	1.67 (0.55 - 5.02)	0.615
Cancer	5 (41.7)	2 (16.7)	7 (29.1)	0.99 (0.38-2.57)	0.178
Surgery	11 (91.7)	4 (33.3)	15 (62.5)	3.00 (1.22 - 7.34)	0.003 < 0.05
Chronic kidney disease	0 (0)	0 (0)	0 (0)	-	-
Chronic Heart disease	0 (0)	0 (0)	0 (0)	-	-
Bed sores	2 (16.7)	0 (0)	2 (8.3)	1.32 (0.26 - 6.53)	0.140
Central venous catheter	5 (41.7)	8 (66.7)	13	2.41 (1.00 - 5.80)	0.219
Nasogastric tube	10 (83.3)	10 (83.3)	10 (83.3)	1.03 (0.32 - 3.30)	1.00
Endotracheal tube or tracheostomy	2 (16.7)	0 (0)	2 (54.1)	0.81 (0.17 - 3.85)	0.140
Antibiotic use	5 (41.7)	1 (8.3)	6 (25)	0.639 (0.23 - 1.71)	0.059
Steroid use	4 (33.3)	3 (25)	7 (29.1)	2.09 (0.78 - 5.62)	0.653

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; OR, odds ratio; SD, standard deviation.

<sup>a</sup>The mean was compared using a t-test.

<sup>b</sup>The median was calculated and compared using the Mann-Whitney U test.

**Table 2.** Comparison of Carriage Rates of MSSA and MRSA Between the Different Wards From Which Patients Were Transported to the ICU

Wards	Total of Subjects No. (%)	No. (%) of Subjects		P Value	OR (95% CI)
		MRSA	MSSA		
Surgical	67 (40.9)	3 (25)	8 (66.7)	0.041	0.167 (0.028 - 0.983)
Emergency room	58 (35.4)	7 (58.3)	2 (16.7)	0.035	7.00 (1.04 - 46.94)
Others	39 (23.8)	2 (16.7)	2 (16.7)	1.000	1.00 (0.117 - 8.559)

Abbreviations: CI, confidence interval; OR, odds ratio.

showed that the MRSA-colonized patients (median age: 63 years) were older than the MSSA-colonized patient (median age: 55 years) (7). Potential factors for the increased rate of MRSA colonization at higher age could be the presence of virulence factors and higher bacterial burdens at the colonized sites.

Since a prior hospitalization may have decreased the rate of MRSA colonization (20), longer HLS before transfer to the ICU may have the same effect in this study. We did in fact find that patients with MRSA colonization had longer hospital stays than MSSA colonized patients. In the study by Warren et al., it was also shown that HLSs prior to admission that were five days or longer posed a more predominant risk associated with MRSA colonization upon admis-

sion (21).

The results from the current study showed that in patients with COPD, colonization with MRSA was identified. However, MSSA colonization was not observed. With findings consistent with our results, Chen and colleagues reported that patients with COPD ( $P = 0.022$ ) are associated with MRSA colonization (5). Although it is controversial, antibiotic therapy is frequently prescribed for COPD and may lead to antibiotic resistance to certain bacteria in these patients.

Prolonged contact with the healthcare setting in patients that have undergone surgery increases the possibility for acquiring *S. aureus*, especially MRSA, from other patients. Thus, as the contact becomes longer and the patient

becomes more ill, a greater concern emerges (19). Moreover, in our study we found that patients undergoing a surgical procedure and then being transferred to the ICU from the surgical ward were more often colonized with MRSA. On the other hand, patients that were transferred to the ICU from the emergency room were mostly colonized with MSSA. Emergency room patients are more representative of the general community, and ergo, they may more often be MSSA colonized. Unfortunately, in our study, there is no record showing that the patients were either directly admitted from the community or from other health-care facilities.

In conclusion, 7.3% of ICU adult patients at our hospital were colonized with MRSA, and patients with certain risk factors, particularly the elderly, had long HLSs before being transferred to the ICU. Furthermore, COPD and surgery were associated with MRSA colonization. We suggest routine MRSA screening upon ICU admission, especially for patients with risk factors. Furthermore, our results showed that extra-nasal MRSA screening upon ICU admission for adult patients can increase the chance of MRSA detection in comparison to nares screening alone.

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### Footnotes

**Authors' Contribution:** Study concept and design, Saeed Abbasi, Soodabeh Rostami, and Farzin Khorvash; acquisition of data, Soodabeh Rostami, Narges Khomarbaghi, and Dariush Shokri; analysis and interpretation of data, Soodabeh Rostami and Nasim Ebrahimi; drafting of the manuscript, Soodabeh Rostami and Nasim Ebrahimi; critical revision of the manuscript for important intellectual content, Saeed Abbasi and Farzin Khorvash; statistical analysis, Soodabeh Rostami; administrative, technical, and material support, Dariush Shokri; study supervision, Saeed Abbasi and Soodabeh Rostami.

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