

# Prevalence and characteristics of methicillin-resistant *Staphylococcus aureus* in community residents of Japan

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## Abstract

**Background:** To implement effective precautions to avoid methicillin-resistant *Staphylococcus aureus* (MRSA) nosocomial infections, it is important to clarify when, how, and from whom MRSA was transmitted to the patients. However, MRSA strains obtained from outpatient population were not analyzed, and the transmission routes of MRSA in the community are not completely understood. The purpose of this study was to clarify whether MRSA is spreading in community settings or whether MRSA transmission still occurs only in healthcare institutions.

**Methods:** Surveillance cultures of 1274 residents living in a community were performed in two different areas, Kochi and Osaka prefectures of Japan. All isolated MRSA strains were evaluated using multilocus sequence typing (MLST) to clarify the transmission routes of MRSA. The results were compared with those of inpatients. Moreover, written questionnaires and medical records were analyzed.

**Results:** Analysis of surveillance cultures from residents living in the community in Japan revealed an MRSA colonization rate of 0.94%. The proportion of MRSA to *S. aureus* colonization was 2.6% in the 310 residents, which was significantly lower than in the 393 hospitalized patients (63.1%;  $P < .0001$ ). MRSA strains in residents are different from the endemic strains in the hospitalized patients. Previous hospital admission is a risk factor for MRSA infection of the endemic strain in hospital.

**Conclusions:** Methicillin-resistant *Staphylococcus aureus* colonization in community setting is rare in Japan. MLST results suggest that some MRSA strains are moving to the community through previous hospital admissions; however, MRSA is not spreading in community settings.

## KEYWORDS

community, infection control, MRSA, multilocus sequence typing, surveillance

## 1 | INTRODUCTION

Control of nosocomial infections remains a major clinical concern to improve mortality and morbidity rates. Methicillin-resistant

*Staphylococcus aureus* (MRSA) continues to be a major nosocomial pathogen since its discovery in 1961. MRSA bacteremia, skin, and soft tissue infection, as well as surgical site infection are associated with longer hospitalization, greater mortality, and higher healthcare

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costs.<sup>1</sup> To date, several different hospital-based strategies have been proposed by infection control personnel and hospital administrators to mitigate the spread and impact of MRSA. However, the incidence of MRSA infection remains virtually consistent.

To implement effective precautions to avoid MRSA nosocomial infections, it is important to clarify when, how, and from whom MRSA was transmitted to the patients. Prior hospital admission is a known risk factor for MRSA infection, which suggests that MRSA infection may have been acquired during prior admission.<sup>2,3</sup> Therefore, it is possible that MRSA is transmitted from the discharged patients to the healthy people in the community; MRSA has spread from the hospitals to the community. Indeed, community-associated MRSA infection has become prevalent in some countries.<sup>4-6</sup>

If the MRSA is prevalent in the community, it is possible the MRSA are transmitted from the person to the person in the community settings, and that more and more patients have acquired MRSA in the community. However, MRSA strains obtained from outpatient population were not analyzed, and the transmission routes of MRSA in the community are not completely understood. Therefore, it was not clear if MRSA infections were prevalent in the community settings. If MRSA infections were prevalent in outpatient population, the transmission of MRSA outside the hospital may be a common event. Thus, it is difficult to conclude whether the patients acquired MRSA through nosocomial infections.

Multilocus sequence typing has been shown to be useful in clarifying the diversity and epidemiology of MRSA in community as well as healthcare settings.<sup>7-10</sup> The purpose of this study was to clarify whether MRSA is spreading in community settings or whether MRSA transmission still occurs only in healthcare institutions. The prevalence of MRSA colonization among people living in Japan was determined by performing surveillance cultures to identify clinically unrecognized MRSA carriers in the community.

## 2 | MATERIALS AND METHODS

### 2.1 | Study setting and design

This active surveillance study was performed in three different groups in Japan from October 2006 to May 2009. A total of 1274 participants participated in this active surveillance study. There is no overlap within the groups. The first group was composed of 163 patients admitted at Kochi Medical School Hospital, which is a 605-bed tertiary-care general hospital with 13 wards. This group was defined as admission cases. The study was conducted at one of the wards with 50 beds. Samples were taken within 48 hours of admission. Therefore, these samples are considered to be "community." The second group was composed of 317 residents from a rural community in Kochi prefecture close to Kochi Medical School Hospital. The participants of this group were recruited through a club for the elderly in this area. Therefore, they were over 60 years old. The third group consisted of 794 supermarket employees in

Osaka prefecture, which is 500 km away from Kochi prefecture. Therefore, they were under 60 years old. Written questionnaires were used for the first and second groups to obtain data regarding previous hospital admissions of either the participants or their family members in the past 3 years. It took several years to submit the work. However, there are no specific reasons which delayed the progress.

### 2.2 | Collection of MRSA isolated from inpatients

A total of 393 *S. aureus* isolates were collected from the hospitalized patients in Kochi Medical School Hospital from October 2006 to May 2009 as inpatient control. These isolates were obtained through conventional clinically oriented ordered cultures.

### 2.3 | Isolation and identification of *S. aureus* and MRSA

After written informed consent was obtained, bilateral anterior nares cultures of all participants were performed. Nasal swabs were obtained from participants using wet (0.85% NaCl) cotton swabs, which were immediately inoculated on Staphylococcus Medium 110 (BD, Sparks, MD, USA) supplemented with 5% egg yolk (Kyokuto, Tokyo, Japan) and trypticase soy agar containing 5% sheep blood (Nippon BD, Tokyo, Japan). Moreover, selective plates were used for MRSA. The plates were cultured for 48 hours at 36°C. Identification of *S. aureus* was performed using API Staph (Sysmex-bioMérieux, Tokyo, Japan) and *femA* and *femB* gene detection with PCR.<sup>8</sup> The presence of *mecA* gene was confirmed using a real-time PCR assay as previously described.<sup>7</sup>

### 2.4 | Laboratory methods

Methicillin-resistant *Staphylococcus aureus* strains collected from participants during the study period were stored and evaluated. DNA extraction and MLST were performed according to the methods described by Enright et al.<sup>8</sup> Sequence types were determined by accessing the MLST website (<http://www.mlst.net/>). MLST was performed using a 3130 Genetic Analyzer (Applied Biosystems, Carlsbad, U.S.A.). MLST was performed for 78 MRSA strains isolated from hospitalized patients during the study period as well as for all twelve strains isolated in the community. These MRSA isolates were randomly selected based on the availability of the samples. Pantone-Valentine leucocidin (PVL) screening was performed for three MRSA isolates as well as in five *S. aureus* isolates using a real-time PCR approach, as previously described.<sup>11</sup>

### 2.5 | Ethical disclosure

The study protocol was approved by the ethics committee of Kochi Medical School, and written informed consent was obtained from all participants to use the data in this study.

**TABLE 1** Frequency of methicillin-resistant *Staphylococcus aureus* (MRSA) colonization in various settings

	Residents <sup>a</sup> (positive/analyzed)	Admission cases (positive/analyzed)	Hospitalized patients (positive/analyzed)	P-value*
MRSA colonization rate	0.72% (8/1111)	2.5% (4/163)	NA	.035
Proportion of MRSA to <i>Staphylococcus aureus</i>	2.6% (8/310)	NA	63.1% (248/393)	<.0001

NA, data were not available.

<sup>a</sup>Both Kochi and Osaka residents.

\*Chi-squared test.

## 2.6 | Statistical analysis

Frequencies and proportions of MRSA colonization were analyzed using the chi-squared test.

## 3 | RESULTS

Methicillin-resistant *Staphylococcus aureus* colonization was investigated in 1111 residents (both Kochi and Osaka prefectures) and 163 admission cases (Table 1). The proportion of MRSA colonization was significantly lower in the residents (0.72%) than in the admission cases (2.5%;  $P = .035$ ). Analysis of surveillance cultures from 1274 participants living in the community in Japan revealed an MRSA colonization rate of 0.94%. *Staphylococcus aureus* colonization was investigated in 1111 residents, which was found in 310 (27.9%) participants (data not shown). The proportion of MRSA to *S. aureus* colonization was 2.6% in the 310 residents, which was significantly lower than in the 393 hospitalized patients (63.1%;  $P < .0001$ ).

The distribution of MRSA isolates in various situations is summarized in Table 2. Only one isolate (ST8) that was isolated in residents was identical to the one isolated in hospital. In contrast, three of four isolates (ST5 and ST8) that were isolated in admission cases were identical to those isolated in hospital. Taken together, MRSA strains in residents are different from those in hospital, and MRSA strains in admission cases are similar to the endemic strains in the hospitalized patients.

Table 3 summarizes the characteristics of the 12 MRSA isolates from the community. Two strains (ST5 and ST8) which consist of four isolates were identified in both the community and hospital. They were either admission cases or Kochi residents who were living close to the hospital. Three cases were previously admitted to the hospital. In addition, the family member of the other Kochi resident had a hospitalization history. Four strains (ST764, ST509, ST688, and ST608) which consist of eight isolates were identified only in the community. Only one case with ST764 had admission history to the hospital. The other five cases were Osaka residents living far from the hospital. The remaining two cases with ST509 were Kochi residents. However, patients or family members had no previous history of admission. Taken together, these seven isolates were either from Osaka residents or Kochi residents without admission history of patients or family members.

**TABLE 2** Distribution of methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from various situations

	Residents <sup>a</sup>	Admission cases	Hospitalized patients
ST5	0	2	39 (50%)
ST8	1	1	17 (22%)
ST675	0	0	22 (28%)
ST764	3	1	0
ST509	2	0	0
ST688	1	0	0
ST608	1	0	0
Total	8	4	78

<sup>a</sup>Both Kochi and Osaka residents.

All of the four admission cases were previously admitted to the hospital (Table 3). Of the 163 admission cases, 98 were previously admitted to our hospital, and four (4.1%) of them were MRSA-positive. In contrast, all 65 patients who were not previously admitted to our hospital were negative for MRSA colonization. Of the four patients with admission history, three had colonization of ST5, or ST8 which were identified in the hospital. On the contrary, of the three patients without admission history, two acquired ST509 strain which was not identified from the hospitalized patients. These results suggest that previous hospital admission is a risk factor for MRSA infection of the endemic strain (ST5, and ST8) in hospital.

Both *mecA* and PVL genes were analyzed in three MRSA isolates (ST8 and two ST509) as well as in five *S. aureus* isolates in community (Figure 1). The *mecA* gene was identified in all three MRSA isolates. The PVL gene was not identified in any of these MRSA isolates.

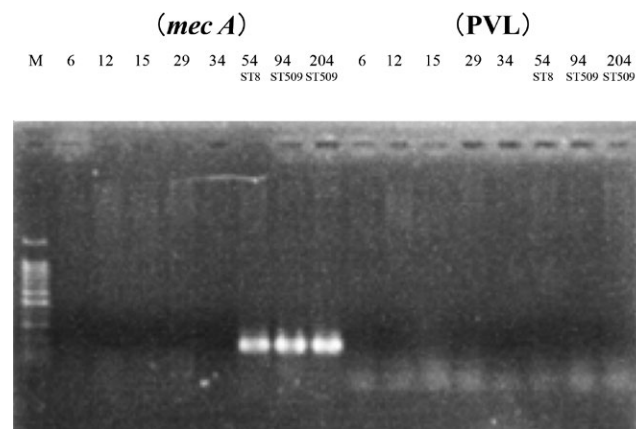
## 4 | DISCUSSION

The epidemiology of asymptomatic MRSA carriers in community settings was analyzed by investigating surveillance cultures of 1111 participants in two areas, Kochi and Osaka prefectures of Japan. The results were compared with those of admission cases and in hospital patients.

Analysis of surveillance cultures from participants living in the community in Japan revealed an MRSA colonization rate of 0.72%. These results are consistent with previous results obtained in the

Isolates	Settings	Previous admission	Hospitalization history of family members	Identification in the hospital
ST5	A	+	NA	+
ST5	A	+	NA	
ST8	K	-	+	+
ST8	A	+	NA	
ST764	A	+	NA	-
ST764	O	NA	NA	
ST764	O	NA	NA	
ST764	O	NA	NA	
ST509	K	-	-	-
ST509	K	-	-	
ST688	O	NA	NA	-
ST608	O	NA	NA	-

A, admission cases; K, Kochi residents; O, Osaka residents; NA, data were not available.



**FIGURE 1** Analysis of *mecA* and Panton-Valentine leucocidin (PVL) genes. Examples are given for eight strains. 6, 12, 15, 29, and 34 are *Staphylococcus aureus*. 54, 94, and 204 are methicillin-resistant *Staphylococcus aureus* (MRSA) and positive for *mecA* gene. None of these MRSA strains were positive for PVL gene. M, DNA ladder

United States and United Kingdom.<sup>12,13</sup> In contrast, prevalence of MRSA colonization in Japanese hospitals is much higher than in hospitals of the United States and United Kingdom.<sup>14,15</sup> This low prevalence rate observed in the present study supports the view that MRSA transmission from the hospitalized patients to the residents of the outside the hospital environment is a rare event. The proportion of MRSA to *S. aureus* colonization was significantly lower in residents (2.6%) than in hospitalized patients (63.1%;  $P < .0001$ ). This also supports the view that MRSA transmission from the hospital to the community environment is rare.

To clarify the origin of MRSA infection, MLST analysis of ninety MRSA isolates was performed. Only one MRSA isolate (ST8) from the residents was identical to that isolated in hospital. In contrast, three (two ST5, and one ST8) of four isolates from the admission cases were identical to those isolated in hospital. Most of the

**TABLE 3** Characteristics of the 12 methicillin-resistant *Staphylococcus aureus* (MRSA) isolates from the community

recently identified MRSA isolates in Japanese hospitals were classified as ST5 or ST8.<sup>7,16</sup> ST764, ST509, ST688, and ST608 were not the endemic strains in the hospitalized patients in Japan.<sup>7,16</sup> Taken together, MRSA strains in residents are different from those in hospital, and MRSA strains in admission cases are similar to the endemic strains in the hospitalized patients. MLST results suggest that the strains which are prevalent in the hospital do not spread to the community.

The results of this study revealed that previous hospital admission is a risk factor for MRSA infection of the endemic strain in hospital, which is concordant with findings from previous studies.<sup>2,3</sup> Our results suggest that residents colonized with MRSA acquired the organism during a previous encounter with our hospital. Therefore, MRSA infection in the community is caused by the MRSA strains originating from hospitals. In other words, MRSA transmissions from the residents to the residents in the community setting are not common. Taken together, preventing MRSA transmission in the community is not a major issue for community health administration.

The present study has several limitations. First, this study was conducted in two areas and in a single medical school hospital in Japan. Therefore, it might be difficult to generalize the status of MRSA circulation in Japan from these results. Second, the positive rate was low to accurately investigate the dynamics of MRSA transmission between community and healthcare settings. Considering the extremely low incidence of MRSA colonization in the community, a significantly larger population sample should be investigated to accomplish the aim of the study. Third, the discriminatory power of MLST may not be sufficient to determine the diversity of MRSA. Inclusion of multiplex PCR-based SCCmec typing would increase the relevance of the data. Finally, we cannot conclude that these MRSA isolates are community-acquired or hospital-acquired, as the PVL gene was analyzed in only three MRSA isolates.

Methicillin-resistant *Staphylococcus aureus* colonization in community setting is rare in Japan. MLST results suggest that some

MRSA strains are spreading in the community through previous hospital admissions; however, MRSA is not spreading in community settings. These results reinforce the central role of infection control precautions in inpatients to prevent nosocomial MRSA transmission.

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## CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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