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ScienceDirect
Diagnostic Microbiology and Infectious Disease 60 (2008) 347–350
DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASE
www.elsevier.com/locate/diagmicrobio

# Injecting drug use and community-associated methicillin-resistant *Staphylococcus aureus* infection

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Received 4 May 2007; accepted 8 November 2007

**Abstract**

To demonstrate that injecting drug use is a major risk factor of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infection and injecting drug users may be a reservoir of CA-MRSA infection in our community, we conducted a matched case-control study. Cases were CA-MRSA–infected patients at University of California, Davis, Medical Center, Sacramento, CA, from December 1, 2003, to May 31, 2004. Two control groups were community-associated methicillin-susceptible *S. aureus* (CA-MSSA)-infected patients and a randomly selected uninfected patient group in the same hospital. Controls were matched to cases by age and isolate culture date. One hundred twenty-seven CA-MSSA patients and 381 randomly selected uninfected controls were selected to match the 127 CA-MRSA cases. The adjusted odds ratio of injecting drug use compared with the CA-MSSA group was 2.11 (95% confidence interval [CI], 1.1–4.3) and 4.09 (95% CI, 2.2–7.5) compared with the uninfected group. We suggest that injecting drug use is a significant risk factor for CA-MRSA infection, which could contribute to the increasing prevalence of CA-MRSA in an urban community.


*Keywords:* CA-MRSA; Injecting drug user; Skin and sift tissue infection

## 1. Introduction

Skin and soft tissue infection (SSTI) is the most prevalent and incident infection among injecting drug users (IDUs). A cross-sectional study (Binswanger et al., 2000) conducted in San Francisco, recruiting 169 IDUs in the community, showed 32% of them had abscess, cellulitis, or both. Other studies have demonstrated that *Staphylococcus aureus* is the most common pathogen causing SSTI in IDUs (Gordon and Lowy, 2005; Summanen et al., 1995). Community-associated methicillin-resistant *S. aureus* (CA-MRSA) infection now accounts for a high proportion of these infections, which can prolong the length of hospital stay and decrease the efficiency of antimicrobial treatment. This may be explained by the higher frequency of nasal and skin colonization with *S. aureus* among IDUs than in the general population (Kluytmans et al., 1997). The pathogen can be introduced into the subcutaneous tissue through damaged skin during injection or into the bloodstream during intravenous injection.

One population-based study (Charlebois et al., 2002) conducted among the urban poor of San Francisco indicated that the risk factor "ever used injected drug" was highly related to MRSA in the population studied. This study and our previous research (Huang et al., 2006) with MRSA among IDU prompted us to further explore the role of IDUs in the epidemiology of CA-MRSA. Our hypothesis is that injecting drug use is a significant risk factor for CA-MRSA infection in our community.

## 2. Methods

A matched case-control study was conducted to evaluate our hypothesis and investigate other potential risk factors of CA-MRSA infection.

### 2.1. Case definition

Cases for this study were patients with newly laboratory-confirmed CA-MRSA isolates identified at University of California, Davis, Medical Center (UCDMC), Sacramento, CA, from December 1, 2003, to May 31, 2004. UCDMC is a

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0732-8893/$ – see front matter © 2008 Published by Elsevier Inc.
doi:10.1016/j.diagmicrobio.2007.11.001

tertiary referral center serving primary care, emergency, and hospitalization needs of the majority of medically uninsured and indigent patients in Sacramento County. The average inpatient census is approximately 450 patients, and its outpatient services experience 2270 visits per day. The definition of "community associated" is a patient whose isolate was cultured within 48 h after admission or as an outpatient; who had no history of hospitalization, surgery, dialysis, or residence in a long-term healthcare facility within 6 months prior to the culture date; and who had no catheters or any other percutaneous medical device present at the time the culture was taken. Patients with duplicate isolates were only evaluated once.

The 2 control groups were individually matched to cases by the isolate culture date and patient age. Patients with the closest age as cases on the same date of culture were substituted if there was no exact age match. The 1st control group was community-associated methicillin-susceptible *S. aureus* (CA-MSSA)-infected patients diagnosed in the same institution. The 2nd control group was composed of randomly selected patients defined as anyone without a documented MRSA infection who had a blood glucose determination done on the same date as the MRSA culture date of the case in the same institution. The ratios of controls to cases were 1 and 3 in CA-MSSA and uninfected control (glucose-test patients) groups, respectively. The glucose test is a regular routine procedure performed on most inpatients and outpatients regardless of the reason of hospital admission or clinic/emergency room visit. This test is not limited to a certain disease or a specific age range. The number of patients having the glucose test performed per day in our institution is approximately 1200. Because of the high proportion of all patients seen at UCDMC, we believe that the uninfected control group adequately represents the general population in the community and also provide a detailed characteristic description of the source population who would seek healthcare in our institution if they were ill.

### 2.2. Data collection

Demographic information, past medical history, length of hospital stay, and social history (including smoking history, alcohol consumption history, and injecting drug use history) were extracted retrospectively by traditional paper chart review and electronic medical chart review. Antimicrobial administration within 30 days before the isolate culture date was recorded as well. The culture site and antimicrobial susceptibility of the isolates were retrieved from microbiology laboratory records at UCDMC. All MRSA cultures were confirmed in the UCDMC microbiology laboratory. Susceptibility testing was performed by the Sceptor system microtiter dilution method (Becton Dickinson, Franklin Lakes, NJ). Susceptibility to cefazolin, clindamycin, ciprofloxacin, erythromycin, gentamicin, oxacillin, rifampin, tetracycline, trimethoprim–sulfamethoxazole, and vancomycin was determined. The results were determined by the guidelines of the Clinical and Laboratory Standards Institute. Double-disk diffusion test (Siberry et al., 2003) was performed on all of the MRSA isolates that were initially defined as resistant to erythromycin but susceptible to clindamycin.

### 2.3. Statistical methods

Statistical analysis was performed by SAS software 8.2 version (SAS Institute, Cary, NC). Univariate analysis was carried out in the initial data analysis step. Continuous variables were analyzed by means of 2-tailed Student's *t* test. Different proportions in groups were compared by $\chi^2$ test or Fisher's exact test if 20% of expected values were smaller than 5. Conditional logistic regression was used to calculate adjusted odds ratio (OR) for potential risk factors. Backward stepwise analysis was performed in the regression model to test the significance of each variable. Variables with $P$ value $\leq 0.15$ were put into the model, as well as those variables, with a biologically plausible relationship with the outcome of interest, regardless of its $P$ value. A $P$ value $<0.05$ was considered statistically significant. This study has been approved by the institution of review board at University of California, Davis.

## 3. Results

A total of 127 CA-MSSA patients and 381 uninfected (glucose test) patients were selected as controls to match the 127 CA-MRSA cases by culture date and age during the study period. The demographic and other baseline characteristics of the study subjects are shown in Table 1. CA-MRSA cases were less likely to have private insurance than CA-MSSA controls (19% versus 57%, $P < 0.001$). A similar result was found while comparing the CA-MRSA patients to uninfected patients (19% versus 58%, $P < 0.001$). The ethnicity distributions of the cases and controls were similar (both $P > 0.05$), although the information was missing for some of our subjects. Among those whose occupation was documented, the proportion of employed patients was lower in CA-MRSA group than in CA-MSSA group (25% versus 55%, $P < 0.001$). Other underlying medical conditions, including chronic viral hepatitis (9% versus 14%), cancer (3% versus 4%), and diabetes (17% versus 12%), did not vary between CA-MRSA and CA-MSSA groups (for all comparisons, $P > 0.2$).

*S. aureus* infection sites were overall similar between CA-MRSA and CA-MSSA groups (Table 2), though CA-MSSA accounted for more episodes of urinary tract infection ($P < 0.001$) than CA-MRSA infection. Subjects with CA-MRSA SSTI did not differ from those with CA-MSSA SSTI with respect to gender ($P = 0.23$) and ethnicity ($P = 0.36$) but had a significantly higher proportion with an injecting drug use history compared with those with CA-MSSA SSTI (43% versus 16%, OR = 4.0, 95% confidence interval [CI] 1.9–8.3, $P < 0.01$). The antimicrobial susceptibility result found