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Protective Effect of Methicillin-Susceptible *Staphylococcus aureus* Carriage against Methicillin-Resistant *S. aureus* Acquisition in Nursing Homes: A Prospective Cross-Sectional Study

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OBJECTIVE. To evaluate whether an ecologic inverse association exists between methicillin-susceptible Staphylococcus aureus (MSSA) prevalence and methicillin-resistant S. aureus (MRSA) prevalence in nursing homes.

METHODS. We conducted a secondary analysis of a prospective cross-sectional study of S. aureus prevalence in 26 nursing homes across Orange County, California, from 2008-2011. Admission prevalence was assessed using bilateral nares swabs collected from all new residents within 3 days of admission until 100 swabs were obtained. Point prevalence was assessed from a representative sample of 100 residents. Swab samples were plated on 5% sheep blood agar and Spectra MRSA chromogenic agar. If MRSA was detected, no further tests were performed. If MRSA was not detected, blood agar was evaluated for MSSA growth. We evaluated the association between MRSA and MSSA admission and point prevalence using correlation and linear regression testing.

RESULTS. We collected 3,806 total swabs. MRSA and MSSA admission prevalence were not correlated ($r = -0.40$, $P = .09$). However, MRSA and MSSA point prevalence were negatively correlated regardless of whether MSSA prevalence was measured among all residents sampled (r p -0.67, $P = .0002$) or among those who did not harbor MRSA (r p -0.41, $P = .04$). This effect persisted in regression models adjusted for the percentage of residents with diabetes (b p -0.73, $P = .04$), skin lesions (b p -1.17, $P = .002$), or invasive devices (b p -1.4, $P=.0006$).

CONCLUSIONS. The inverse association between MRSA and MSSA point prevalence and minimal association on admission prevalence suggest MSSA carriage may protect against MRSA acquisition in nursing homes. The minimal association on admission prevalence further suggests competition may occur during nursing home stays.

Nursing homes are a growing reservoir for methicillin-resistant *Staphylococcus aureus* (MRSA). We and others have previously reported that MRSA prevalence ranges from 5% to 50% in skilled nursing facilities,[1-6] and transmission is com- mon.[7-11] Residents have many risk factors for MRSA acquisition, including chronic diseases, exposure to antibiotic therapy and invasive devices, presence of wounds, and frequent sharing of rooms and common areas.[12-16] Environmental contamination and infrequent use of contact precautions may further predispose to MRSA acquisition in nursing home residents.[17]

MRSA acquisition is important due to the high risk of subsequent infection. Up to one-third of chronically ill patients experience invasive disease in the year following acquisition, and substantial risk persists even in those colonized for some time.[18,19] This high risk of infection has heightened the importance of preventative factors to reduce MRSA acquisition. Earlier studies suggest that methicillin-susceptible *S. aureus* zed (MSSA) colonization may protect against MRSA acquisition in hospitals.20,21 This protective effect may be particularly relevant as the use of decolonization regimens in- creases.22-26 These topical regimens, such as the national guideline for preoperative screening and decolonization of *S. aureus* among patients preparing for cardiac surgery23 and use of daily chlorhexidine bathing in intensive care units,25,27 tar- get both MRSA and MSSA. These treatments may create a vacated anterior nares niche that poses an increased risk of MRSA acquisition or recolonization, particularly when patients are discharged to settings with a high MRSA prevalence, like nursing homes.

The preference for MSSA over MRSA colonization in set- tings with a high prevalence of MRSA may be justified by the known higher risk of disease among MRSA carriers than MSSA carriers.28 One meta-analysis suggested that MRSA carriage is associated with a fourfold greater infection risk com- pared with MSSA carriage, a risk that persisted even after controlling for host risk factors.29,30 Furthermore, although MSSA infections may be severe, MRSA infections are associated with greater morbidity and mortality than MSSA infections.31-34 Due to the high prevalence and transmission of MRSA in nursing homes, we sought to assess whether an ecological

inverse association exists between MRSA and MSSA prevalence in nursing homes after controlling for host factors known to predispose to MRSA acquisition.

TABLE 1. Facility-Level Descriptive Characteristics of Participating Nursing Homes (n = 26) in Orange County, California

Facility-level characteristic	Median (range)
Nursing home volume	
No. of beds	99 (24–255)
No. of annual admissions	262 (18–1,526)
Length of stay, median (range), days	101 (17–753)
Demographic characteristics, % of nursing home residents	
Age <65 years	14 (0–75)
Age >85 years	25 (2–72)
Male sex	42 (21–67)
Hispanic ethnicity	17 (1–38)
Nonwhite race	16 (1–88)
Education less than high school	24 (0–64)
Medicaid insurance	18 (1–44)
Diabetes	27 (11-59)
Skin lesion	72 (4–100)
Indwelling device	2 (0–46)
Fecal incontinence	44 (5–91)
Poor locomotion	60 (14–89)
Mean social engagement score	2 (0–4)

METHODS

We previously conducted a prospective cross-sectional study of admission prevalence and point prevalence of *S. aureus* among residents of 26 nursing homes in Orange County, California, between October 2008 and May 2011.[5] We previously reported MRSA prevalence and now evaluate a secondary analysis assessing the relationship between MRSA and MSSA carriage.[5] Study procedures have been described.[5] Briefly, bilateral nares swab samples from all incoming res- idents were collected within 3 days of admission until 100 swab samples were obtained per facility. For nursing homes with infrequent admissions, a smaller sample of 30-50 residents was screened. For nursing homes with rare admissions (average length of stay in years), admission screening was not performed. MRSA and MSSA point prevalence was obtained from bilateral nares swab samples from a representative sample of 100 residents in consecutive rooms per nursing home on a single day. If fewer than 100 residents were available, additional screenings were performed separated by a mini mum of twice the average length of stay from the previous screening. Point prevalence sampling occurred after 7 days of admission and prospectively thereafter. This study was approved by the institutional review board of the University of California Regents.

Bilateral nares specimens were cultured onto both 5% sheep blood agar (BBL) and Spectra MRSA agar (Remel). If MRSA was not detected on Spectra agar, but growth resembling *S. aureus* was noted on blood agar, colonies were identified and confirmed as either MSSA or MRSA. MRSA-positive specimens on Spectra agar were not evaluated for MSSA co-colonization.

To assess the frequency of MRSA and MSSA co-colonization, bilateral admission nares specimens from a tertiary care referral center for participating nursing homes were evaluated between September 2011 and February 2012. Here, in addition to the methodology described above, if MRSA was isolated from Spectra agar, the corresponding blood agar was evaluated for growth. If the amount of growth was greater than that on Spectra agar, the organisms were identified as MRSA or MSSA. Additionally, if different colony morphologies were present on sheep blood agar that

resembled *S. aureus*, the different colony types were tested for MRSA or MSSA.

We collected multiple facility-level variables for participating nursing homes using the minimum data set and publicly available data, including the proportion of residents who were male, less than 65 years of age, greater than 85 years of age, nonwhite, Hispanic ethnicity, and Medicaid-insured as well as the proportion of residents with diabetes, skin lesions, indwelling devices, fecal incontinence, and poor locomotion.35,36 We further determined the number of beds, annual admissions, cumulative resident-days, and social engagement score.37 Individual-level data for sampled residents were not collected.

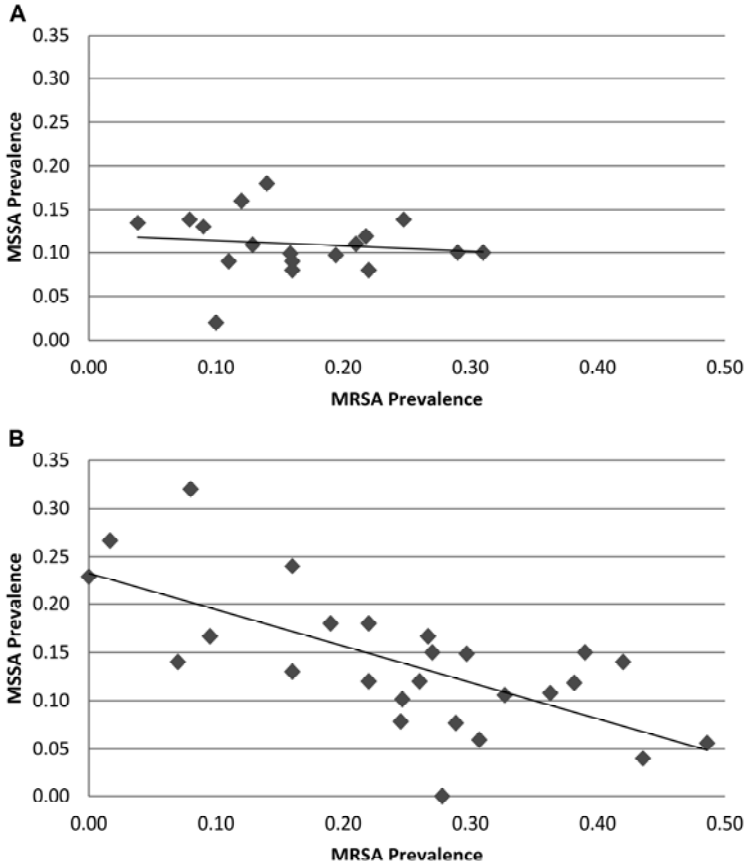

FIGURE 1. *A*, Prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-susceptible *S. aureus* (MSSA) among residents at admission to participating nursing homes in Orange County, California. Diamonds represent MRSA and MSSA admission prevalence at participating nursing homes. Admission prevalence swab samples were unavailable in 7 facilities where the mean length of stay among residents was measured in years. One outlier facility was excluded. *B*, Point prevalence of MRSA and MSSA among residents in participating nursing homes in Orange County, California. Diamonds represent MRSA and MSSA point prevalence at participating nursing homes.

We evaluated the association between MRSA and MSSA admission prevalence and MRSA and MSSA point prevalence at the facility level using tests of correlation. To account for the possibility of co-colonization, we evaluated the association between overall MRSA prevalence and MSSA prevalence when measured among all residents sampled as well as among the subset of residents who did not harbor MRSA on Spectra MRSA agar. We further evaluated the fraction of MRSA-positive nares specimens that simultaneously grew MSSA from the above-mentioned sample of hospitalized patients.

To assess the protective effect of MSSA carriage against MRSA acquisition, we evaluated the impact of MSSA prevalence on MRSA prevalence when controlling for select facility-level factors previously shown to predispose to MRSA acquisition. These factors included the proportion of residents with diabetes, skin lesions, fecal incontinence, and indwelling devices as well as resident social engagement score.12-14 Variables significant at *a* p 0.1 in bivariate testing using linear regression models were entered into a multivariate facility-level linear regression model (SAS, version 9.3). Given the

sample size, multivariate models were restricted to MSSA point prevalence and 1 additional facility-level variable to prevent overfitting.

RESULTS

Of the 72 total nursing homes in Orange County, 26 facilities (36%) agreed to participate in this study. As previously reported, 5 we obtained 1,661 admission samples and 2,145 point prevalence samples between 2008 and 2011. Admission nares samples from 7 nursing homes were not obtained due to small facility size and prolonged length of stay. Descriptive characteristics of participating nursing homes are summarized in Table 1. Point prevalence sampling occurred a median of 7 months (range, 2–16 months) after admission. In 38% of nursing homes, point prevalence measurements were obtained from all residents.

When evaluating imported S. aureus prevalence across nursing homes, the median admission prevalence of MRSA and MSSA was 16% (range, 3%–31%) and 11% (range, 2%–34%), respectively. There was no significant correlation between MRSA and MSSA prevalence upon nursing home admission(r = -0.40, P = .09), with minimal variability (2%) in MRSA admission prevalence attributable to changes in MSSA admission prevalence (R2 p 0.02; Figure 1A).

In contrast, when evaluating S. aureus prevalence among current nursing home residents, we found that the median point prevalence of MRSA and MSSA was 27% (range, 2%–49%) and 14% (range, 4%–32%), respectively, and there was a significant inverse correlation when comparing MRSA point prevalence to MSSA point prevalence (r = -0.67, P = .0002). In contrast to admission findings, nearly 50% of the variability in MRSA point prevalence was attributable to changes in MSSA point prevalence after admission (R2 = 0.45; Figure 1B). This inverse correlation between MRSA and MSSA prevalence persisted when limiting MSSA point prevalence to those residents who did not harbor MRSA (r = - 0.41, P = .04).

When assessing the frequency of MRSA and MSSA co-colonization among the sample of hospital-based nares samples submitted for MRSA screening, 1,294 (9%) of 14,894 cultures grew MRSA. Of these, MSSA co-colonization was found in only 1.9% (n = 24) of screening cultures.

Facility-level characteristics associated with MRSA point prevalence in bivariate testing are shown in Table 2. In multivariate regression testing, MSSA point prevalence remained inversely associated with MRSA point prevalence regardless of whether accounting for the percent of residents with diabetes (b = -0.73 [95% confidence interval (CI), _1.4 to -0.03]; P = .04), skin lesions (b = -1.17 [95% CI, -1.9 to -0.5]; P = .002), invasive devices (b = -1.4 [95% CI, -2.1 to -0.67; P = .0006), or fecal incontinence (b = -0.86 [95% CI, -1.5 to -0.16]; P = .02).

DISCUSSION

In this ecologic study of *S. aureus* in 26 nursing homes, we found an inverse association between the facility-level prevalence of MRSA and MSSA during point prevalence sampling of nursing home residence but not upon admission. These findings suggest that MRSA acquisition is independent of MSSA carriage at the time of nursing home admission, but during nursing home residence, MRSA and MSSA exert robust competition for colonization of the nasal reservoir. MSSA carriage may thus confer a protective effect against MRSA acquisition in nursing homes and contributes to the growing body of evidence indicating that *S. aureus* strains compete for colonization of the anterior nares.20, 21

The lack of correlation in the proportion of residents with MRSA and MSSA upon admission would be expected for patients arriving independently from various hospitals around the county. In contrast, the strong inverse correlation in MRSA and MSSA point prevalence may reflect the impact of social interaction on opportunities for *S. aureus* trans- mission while residing at the nursing home. Overall, we observed a 7%–14% reduction in MRSA point prevalence per 10% increase in MSSA point prevalence after accounting for resident comorbidities.

Our findings may be relevant to the increasing practice of decolonization with mupirocin and chlorhexidine to prevent healthcare-associated infections in hospitals.22,24,25-27 Decolonization in intensive care unit settings is increasingly com- mon, and cardiac and orthopedic surgeons commonly de-colonize *S. aureus* carriers before surgery.23 These and other decolonization practices have the potential to clear the nasal reservoir, thereby predisposing patients to MRSA acquisition in nursing homes, where roughly one-third of residents harbored MRSA in our study. Future studies are needed to balance the risks of *S. aureus* infection during the hospital stay with the potential for increased MRSA acquisition

when dis- charged to long-term care settings where MRSA is endemic. These risks may also be mitigated by decolonization efforts in nursing homes.

This ecologic study has important limitations. First, the cross-sectional design of this study precludes the assessment of the temporal sequence of colonization. As a result, it is unknown whether MSSA colonization prevents MRSA acquisition or whether another explanation exists. For example, if antibiotic usage in nursing homes preferentially cleared MSSA carriage, it would cause MRSA and MSSA prevalence to appear inversely correlated. However, the fact that several nursing homes exhibit a higher MSSA point prevalence com- pared to admission prevalence would make this explanation less likely. Second, because nursing home participation was predicated on minimal collection of resident-level data, we could only evaluate facility-level population characteristics. Third, we did not evaluate extranasal colonization with MRSA and MSSA, although it may be common among nursing home residents.4 Fourth, we did not perform strain typing to distinguish between transient and persistent colonization. We also did not evaluate facility practices that may impact *S. aureus* prevalence, although nursing homes did not perform decolonization during the study period. Additionally, our findings may be partially explained by increased MRSA transmissibility. However, infection prevention methods were al- ready implemented at participating nursing homes to limit transmission. Finally, MRSA and MSSA co-colonization was not assessed among residents. However, our data from a representative sample of inpatients and earlier literature suggest that co-colonization is rare.20

In summary, we found an inverse association between MRSA and MSSA prevalence across nursing homes in a large metropolitan county. This suggests that MSSA carriage may confer a protective effect against MRSA acquisition during nursing home residence. Additional studies are needed to directly assess whether MSSA carriage may prevent the acquisition of MRSA in nursing homes, including whether previous decolonization increases the risk of MRSA acquisition or recolonization in settings in which MRSA is highly endemic, such as nursing homes.

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