The Intersecting Epidemics of Human Immunodeficiency Virus, Community-Associated Methicillin-Resistant *Staphylococcus aureus*, and Incarceration

Kyle J. Popovich,[1] Chad Zawitz,[2] Robert A. Weinstein,[1] Amanda E. Grasso,[3] Anna L. Hotton,[3] and Bala Hota[1]

[1]Rush University Medical Center/Cook County Health and Hospitals System, [2]Cermak Health Services and Cook County Health and Hospitals System, and [3]Cook County Health and Hospitals System, Chicago, Illinois

Community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) has had a significant impact on human immunodeficiency virus (HIV)-infected and incarcerated individuals. We examined electronic medical surveillance data from 2006 to 2011 and observed that even in a population of currently or recently incarcerated individuals, HIV status was a significant risk factor for MRSA infections and Hispanic ethnicity was protective.

Keywords. HIV; incarceration; MRSA.

The epidemics of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA), human immunodeficiency virus (HIV)/acquired immune deficiency syndrome, and incarceration have intersected with striking clinical consequences [1, 2]. Human immunodeficiency virus-infected individuals have a higher incidence of CA-MRSA skin and soft tissue infections [1] and a higher prevalence of CA-MRSA colonization compared with HIV-negative individuals [3, 4]. A study examining the prevalence of nasal MRSA colonization among HIV-infected and HIV-negative outpatients in Chicago showed the highest prevalence of colonization among HIV-infected individuals with recent incarceration [4]. Hispanic ethnicity has been negatively associated with CA-MRSA colonization [3] and infection [5], even among the HIV-infected [4].

It is unclear why there is differential risk for CA-MRSA based on HIV status and ethnicity, although it has been speculated that differences in incarceration exposure, residence, and social networks may affect risk [3, 4]. This study's objective was to determine whether previously described disparities in MRSA risk persisted in a large study population in which everyone had current or recent incarceration.

METHODS

Study Population

Using existing medical electronic surveillance data from the Cook County Health and Hospitals System (CCHHS), we evaluated individuals 18 years of age or older with current or recent incarceration at the Cook County Jail, the largest single-site US jail (average census of 10 000 detainees; 70 000–100 000 annually) and the major jail in Cook County, Illinois. We performed a case-control study to determine epidemiologic factors associated with MRSA-positive clinical cultures. Individuals were identified who had an MRSA-positive clinical culture from January 2006 to December 2011 while a detainee or within 6 months of jail release (Cases). Six months was used as a conservative measure of the duration of *S aureus* colonization [6, 7] that could potentially be attributed to the jail. Controls were individuals who were incarcerated during the study period but who did not have MRSA isolated during this time frame, including the 6 months postrelease. Four controls were randomly sampled from the population of jail detainees for every case identified. Individuals had the opportunity to be classified as a case for each episode of incarceration, and clinical cultures separated by 30 days or more were counted as separate events.

Culture Data

Microbiologic cultures were those obtained at hospitals and outpatient clinics in CCHHS, the safety-net healthcare network in Cook County, Illinois—Stroger (formerly Cook County) Hospital (the major public hospital in Cook County), Cook County Jail, Provident Hospital, Oak Forest Hospital, and affiliated ambulatory care centers. Culture data from the Cook County Jail were available from 2010 to 2011; other hospital and ambulatory sites had culture data for the entire study period. No nares cultures were included; all included isolates are from clinical cultures.

Statistical Analysis

Analysis was performed using SAS software version 9.2 (SAS Institute, Cary, NC). Cases and controls were compared using

Received 11 August 2015; accepted 27 September 2015.

Correspondence: Kyle Popovich, MD, MS, 1900 West Polk Street, 12th floor, Chicago, IL (kyle_popovich@rush.edu).

Open Forum Infectious Diseases

DOI: 10.1093/ofid/ofv148

Table 1. Univariate and Multivariable Analysis of Factors Associated With Methicillin-Resistant *Staphylococcus aureus*-Positive Clinical Cultures[a]

	Univariate Analysis				Multivariable Analysis	
Factor[b]	MRSA Clinical Cases (n = 390)	Controls (n = 1800)	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Gender						
Male	327 (84%)	1545 (86%)	0.86 (.6–1.2)	.31	—	—
Female	63 (16%)	255 (14%)				
Age in years, mean (SD)	36.1 (11.5)	33.5 (11.1)	1.02 (1.01–1.03)	<.001	1.02 (1.01–1.03)	<.001
Race/Ethnicity						
Non-Hispanic Black	269 (69%)	1207 (68%)	1.4 (1.02–2)	.04	1.4 (.9–2)	.12
Non-Hispanic White	71 (18%)	256 (14%)	1.8 (1.2–2.6)	.01	2 (1.3–3.1)	.003
Hispanic	48 (12%)	305 (17%)	Reference	—	Reference	—
HIV Infection	32 (8%)	36 (2%)	4.4 (2.7–7.1)	<.001	4.4 (2.7–7.4)	<.001
Repeat incarceration during study period	28 (7%)	39 (2%)	3.5 (2.1–5.8)	<.001	3.7 (2.2–6.2)	<.001
Median jail length of stay, in days	30 (1181)	16 (1637)	1.002 (1.001–1.003)	<.001	1.4 (1.3–1.5)	<.001

Abbreviation: CI, confidence interval; HIV, human immunodeficiency virus; MRSA, methicillin-resistant *Staphylococcus aureus*; OR, odds ratio; SD, standard deviation.

[a] Data for univariate analysis are no. (%) of individuals, unless otherwise indicated.

[b] Ethnicity data were missing for 34 individuals, and therefore the denominator for the race/ethnicity variable for univariate analysis is 2156. Individuals labeled as both non-Hispanic and "other" race comprised 0.5% of the total study population; these individuals were included as non-Hispanic whites. For the jail-length-of-stay variable, 54 individuals had not been discharged from the jail at end of the study period, and therefore the denominator for this variable for univariate analysis is 2136. The jail-length-of-stay variable was highly skewed, and a natural log transformation was applied to improve the symmetry of the distribution and model fit. For univariate analysis, the median jail length of stay in days transformed to natural log was 3.4 (range 7) for cases and 2.8 (range 7) for controls (OR = 1.4; 95% CI, 1.3–1.5; $P < .001$). Initial variables included in the model were as follows: gender, age, jail length of stay, HIV, repeat incarceration, race/ethnicity. The Hosmer-Lemeshow goodness-of-fit test, $P = .24$.

χ^2 tests for categorical variables, Fisher's exact test for small samples, and the independent-samples *t* test for continuous variables. The Wilcoxon rank-sum test was used to compare time until MRSA-positive clinical culture across levels of exposure variables. Logistic regression was used for univariate and multivariable analysis of factors associated with MRSA-positive clinical cultures. Statistically important variables on univariate analysis ($P < .2$) were entered into the multivariable model. A backward elimination approach was used for modeling with $P < .05$ as the cutoff for retention in the final model. Confounding and effect modification was assessed, and the Hosmer-Lemshow Goodness-of-fit test was performed on the final model. Because culture data from the Cook County Jail were only available from 2010 to 2011, we performed a sensitivity analysis for this time period. The study was approved by the Institutional Review Boards of Rush, CCHHS, and the Office for Human Subjects Protections.

RESULTS

From January 2006 through December 2011, there were 390 patients with MRSA-positive clinical cultures during incarceration or within 6 months of release; 1800 controls were identified. Most cultures were obtained from skin and soft tissue sites (75%). Human immunodeficiency virus infection was significantly associated with MRSA-positive clinical cultures (odds ratio [OR] = 4.4; 95% confidence interval [CI], 2.7–7.1; $P < .001$). Older age, repeat incarceration during the study period, and longer length of incarceration were associated with MRSA-positive clinical cultures on univariate analysis (Table 1). Females had a significantly shorter time until an MRSA-positive clinical culture while incarcerated than did males (35 days vs 82 days, $P = .04$). Hispanic ethnicity was negatively associated with MRSA-positive clinical cultures (OR = 0.69; 95% CI, .5–.95; $P = .02$). Median length of stay in the jail did not differ between males and females or between Hispanics and others.

On multivariable analysis, HIV infection remained a significant factor associated with MRSA-positive clinical cultures (OR = 4.4, 95% CI, 2.7–7.4; $P < .001$), even after adjusting for demographic factors and length of stay in the jail. In addition, Hispanic ethnicity remained negatively associated with an MRSA-positive clinical culture (Table 1). In our sensitivity analysis for the years 2010–2011, we observed that HIV, length of incarceration, and race/ethnicity all remained significant factors associated with MRSA-positive clinical cultures. When year of incarceration was included in the model, the magnitude, direction, and significance of effects were largely unchanged.

There was a total of 68 HIV-infected individuals, of whom 32 (47%) had an MRSA-positive clinical culture during the study period. Most HIV-infected individuals were male (76%) and

African-American (84%). CD4 count data was available for 47% of HIV-infected individuals. Median CD4 count did not differ among patients with and without MRSA-positive clinical cultures (259 vs 249 cells/mm^3; $P = .9$). The mean CD4 count also did not differ between those individuals with and without MRSA-positive clinical cultures (291 vs 282 cells/mm^3; $P = .9$). There was a trend toward more HIV-infected women having an MRSA-positive clinical culture than HIV-infected males (11 of 16, 69% vs 21 of 52, 40%; $P = .08$). Human immunodeficiency virus-infected individuals were significantly more likely to have repeat episodes of MRSA-positive clinical cultures (OR = 4.6; 95% CI, 1.7–12.1; $P = .008$) and repeat incarceration (OR = 5.4; 95% CI, 2.6–11.5; $P < .001$) compared with HIV-negative individuals. Median length of incarceration per episode was not significantly different for HIV-infected individuals ($P = .6$).

DISCUSSION

Prior work has suggested that incarceration or exposure to high-risk social networks after incarceration may contribute to differential risk for CA-MRSA colonization and infection in certain populations [3, 4]. However, we observed that even in a population where everyone had current or recent exposure to a large inner-city jail, HIV infection remained a significant independent predictor of MRSA; Hispanic ethnicity remained protective (Table 1).

The current study reinforces the significant interaction of HIV status and incarceration exposure [3, 4]. Almost 50% of HIV-infected individuals in the study developed an MRSA infection, underscoring the high burden and MRSA risk among HIV-infected, incarcerated individuals. Human immunodeficiency virus-infected individuals were more likely to have multiple episodes of incarceration, which may create opportunities for repeated exposure to a reservoir of individuals with a high burden of MRSA. Although CD4 count has not been associated with increased risk for MRSA [2], it is unclear whether immune or mucosal factors contribute to the disproportionate burden of MRSA among HIV patients, particularly in a high-risk MRSA environment such as a correctional facility.

Prior studies have speculated that social factors such as prevalence of incarceration, location of residence, and social networks may contribute to the reduced MRSA risk observed among Hispanics [3, 4]. To assess whether incarceration exposure served as the basis for this differential risk, we restricted the study population to current or recent detainees at the jail. We observed that even in this high-risk population, Hispanic ethnicity was negatively associated with MRSA, and further evaluation of host factors may be warranted.

Females had a shorter time until developing an MRSA-positive clinical culture in the jail, and a higher proportion of HIV-infected females had an MRSA-positive clinical culture compared with HIV-infected males. A study in the Texas prison system similarly documented that the incidence of MRSA infections was higher among female detainees [8]. It has been speculated that differences in drug use patterns or in types of physical contact in prison facilities account for the observed disparity between male and female [9]. Future research with a larger sample size would be of value to investigate the burden of MRSA among females in disadvantaged patient populations.

Our study has limitations. We did not have access to microbiologic results from the jail for a portion of the study period. In addition, some individuals may have received empiric antibiotic therapy without a culture being obtained, which could lead to misclassification of individuals as controls. However, because this misclassification would bias toward the null hypothesis of no association, this underscores the importance of our associations. In addition, we used a 6-month follow-up period and thus cannot definitively attribute acquisition of postrelease infecting strains to the jail. In addition, we did not examine prior antibiotic and healthcare exposure data and therefore cannot rule out residual confounding in the analysis. Finally, although there are systems in place to assist released detainees with CCHHS follow-up, there is still the possibility that individuals sought postrelease care elsewhere, creating ascertainment bias.

CONCLUSIONS

Our study extends prior work in this field by examining a large population of current or recently incarcerated individuals at a large urban jail over a 6-year time period and demonstrates that HIV status remained a significant risk factor for MRSA infections while Hispanic ethnicity was protective. Our findings support future investigations into environmental and host factors for MRSA infection, particularly in high-risk MRSA settings such as correctional facilities.

Acknowledgments

We thank Dr. Connie Mennella, Chief Medical Officer at Cermak Health Services, for help with this project.

Disclaimer. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Allergy and Infectious Diseases or the National Institutes of Health.

Financial support. This work was funded by Grant Number K23AI085029 (to K. J. P., principal investigator) from the National Institute of Allergy and Infectious Diseases and the Chicago Developmental Center for AIDS Research (P30 AI 082151).

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

References

1. Popovich KJ, Weinstein RA, Aroutcheva A, et al. Clin Infect Dis **2010**; 50:979–87.
2. Shet A, Mathema B, Mediavilla JR, et al. Colonization and subsequent skin and soft tissue infection due to methicillin-resistant *Staphylococcus aureus* in a cohort of otherwise healthy adults infected with HIV type 1. J Infect Dis **2009**; 200:88–93.

3. Popovich KJ, Hota B, Aroutcheva A, et al. Community-associated methicillin-resistant *Staphylococcus aureus* colonization burden in HIV-infected patients. Clin Infect Dis **2013**; 56:1067–74.
4. Popovich KJ, Smith KY, Khawcharoenporn T, et al. Community-associated methicillin-resistant *Staphylococcus aureus* colonization in high-risk groups of HIV-infected patients. Clin Infect Dis **2012**; 54:1296–303.
5. Hota B, Ellenbogen C, Hayden MK, et al. Community-associated methicillin-resistant *Staphylococcus aureus* skin and soft tissue infections at a public hospital: do public housing and incarceration amplify transmission? Arch Intern Med **2007**; 167:1026–33.
6. Lucet JC, Paoletti X, Demontpion C, et al. Carriage of methicillin-resistant *Staphylococcus aureus* in home care settings: prevalence, duration, and transmission to household members. Arch Intern Med **2009**; 169:1372–8.
7. Robicsek A, Beaumont JL, Peterson LR. Duration of colonization with methicillin-resistant *Staphylococcus aureus*. Clin Infect Dis **2009**; 48:910–3.
8. Baillargeon J, Kelley MF, Leach CT, et al. Methicillin-resistant *Staphylococcus aureus* infection in the Texas prison system. Clin Infect Dis **2004**; 38:e92–5.
9. Lowy FD, Aiello AE, Bhat M, et al. *Staphylococcus aureus* colonization and infection in New York State prisons. J Infect Dis **2007**; 196:911–8.