Prevalence and risk factors for MRSA nasal colonization among persons experiencing homelessness in Boston, MA

Jessica H. Leibler,[1,*] Casey León,[2] Lena J. P. Cardoso,[2] Jennifer C. Morris,[1] Nancy S. Miller,[3,4] Daniel D. Nguyen[1] and Jessie M. Gaeta[2,5]

Abstract

Homeless individuals face an elevated risk of methicillin-resistant *Staphylococcus aureus* (MRSA) infection. Identifying the prevalence and risk factors for MRSA nasal colonization may reduce infection risk. A cross-sectional study was conducted at a health clinic for homeless persons in Boston, MA, USA (*n*=194). In-person interviews and nasal swab specimens were collected. MRSA isolates were genotyped using pulse-field gel electrophoresis (PFGE) and assessed for antibiotic susceptibility. The prevalence of MRSA nasal colonization was 8.3 %. Seventy-five percent of isolates reflected clonal similarity to USA300. USA100 (18.8 %) and USA500 (6.3 %) were also recovered. Resistance to erythromycin (81.3 %), levofloxacin (31.3 %) and clindamycin (23.1 %) was identified. Recent inpatient status, endocarditis, haemodialysis, heavy drinking, not showering daily and transience were positively associated with MRSA nasal colonization. Carriage of community-acquired MRSA strains predominated in this population, although nosocomial strains co-circulate. Attention to behavioural and hygiene-related risk factors, not typically included in MRSA prevention efforts, may reduce risk.

Methicillin-resistant *Staphylococcus aureus* (MRSA) infection is associated with significant morbidity and mortality, including skin and soft tissue infection (SSTI), surgical site infections, bacteraemia and endocarditis [1–4]. MRSA organisms, which are resistant to the beta-lactam class of antibiotics and are frequently multidrug resistant, are responsible for the deaths of over 19 000 hospitalized persons in the United States annually [5]. While rates of healthcare-acquired MRSA have decreased in recent years, the incidence of community-acquired infection has remained constant during this period, despite more than two decades of intervention efforts [3]. The risk factors for MRSA infection include recent hospitalization, recent antibiotic use, incarceration, injection drug use and living in crowded conditions [6]. While these risk factors are highly prevalent among persons experiencing homelessness in the United States and other high-income countries [7–9], only limited research to date has been conducted on the characteristics of MRSA in this population [10–15].

Homelessness in high-income countries is a public health problem of growing concern. More than 3.5 million Americans who experienced homelessness in 2013, and 85 % resided in urban centres [16]. Homeless individuals who live in shelters are exposed to crowded living conditions and may lack regular access to clean sanitation facilities and opportunities for hygiene [17, 18]. Unsheltered individuals who sleep on the street also face reduced opportunities for sanitation and hygiene [19]. These environmental conditions pose increased risk for the transmission of infectious agents, notably respiratory pathogens such as tuberculosis, but also contact pathogens such as *S. aureus* that may be mediated by limited hygiene and crowded living conditions [20–24]. Substance use, including injection drug use, is more common among persons experiencing homelessness, [25] and specific injection behaviours, including skin popping, injecting with a family member or partner and intramuscular injection, are associated with elevated risk of *S. aureus* skin infection in this population [26, 27].

In many urban Emergency Departments (EDs), particularly those that treat many low-income and homeless individuals, SSTIs are often treated empirically due to the cost and time involved in diagnostic analyses [28] and follow-up may be limited, complicating efforts to assess treatment success. There is a clear need to inform clinical treatment in this

difficult-to-reach population, and identify specific environmental and behavioural risk factors to reduce infection risk. We conducted a cross-sectional study among non-hospitalized individuals experiencing homelessness to assess the prevalence, antibiotic susceptibility and genotype of MRSA nasal colonization, as well as risk factors that may be specific to homelessness in the United States. MRSA nasal colonization is associated with increased risk of *S. aureus* infection and is a non-invasive biomarker of infection risk [29], with strong evidence of strain concordance between nasal colonization and infection [30].

STUDY DESIGN AND CONDUCT

Participants were recruited over the course of 4 days into a cross-sectional study in July 2015 at Boston Health Care for the Homeless Program (BHCHP), a large healthcare provider for individuals experiencing homelessness in the Boston metropolitan area, using a convenience sampling design and word-of-mouth recruitment. Individuals were eligible to participate if they were current patients at the clinic, currently experiencing homelessness or had been homeless in the last 3 months, older than 18 years and able to speak English. Study participation consisted of a 20 minute semistructured interview using a questionnaire tool and collection of a nasal swab specimen. The questionnaire focused on recent medical history, medical access, hygiene behaviour, substance use, housing status and demographics. All aspects of the study design and conduct were approved by the Institutional Review Board at the Boston University Medical Center.

Following the interview, a nasal swab specimen was collected using a BD Eswab collection kit (BD Diagnostics, Sparks, MD, USA). Nasal specimens were cultured using the manufacturer-specified protocol for Remel Spectra chromagar plates (Remel, Lenexa, KS, USA). MRSA isolates were assessed for susceptibility to eight antibiotics commonly used to treat *Staphylococcus* infections (clindamycin, erythromycin, levofloxacin, penicillin, oxacillin, trimethoprim/sulfamethoxazole, vancomycin and tetracycline) using the VITEK2 automated instrument (bioMérieux, Inc., Marcy l'Etoile, France), which compares bacterial growth to established MIC thresholds [31]. Isolates denoted as 'susceptible' or 'intermediate' on the basis of the MIC cutoffs for each antibiotic were labelled as susceptible. MRSA positivity was defined as culture-positive results from the chromagar plates in conjunction with identified resistance to oxacillin and penicillin from the susceptibility testing. Pulse-field gel electrophoresis (PFGE) was conducted at the Massachusetts State Public Health Laboratory (William A. Hinton State Laboratory Institute, Jamaica Plain, MA, USA) using standard techniques and database comparison to assess clonal similarity to currently circulating strains of MRSA in Boston on the basis of state laboratory records [32]. Analysis of *Sma*I restriction fragments was conducted using the approach outlined by McDougal *et al.* in reference to *S. aureus* [33]. Clonal similarity was evaluated per McDougal in reference to the closest 10 MRSA clones in the database.

Descriptive statistics, including prevalence by demographic group and colonization status, were conducted. Univariate logistic regression was used to assess demographic, behavioural and medical risk factors for MRSA nasal colonization. Multivariable logistic regression models adjusting for age and sex were also utilized to control for these factors.

MRSA NASAL COLONIZATION PREVALENCE

One hundred ninety-four individuals (*n*=194) were enrolled in the study (Table 1). An additional 11 persons were recruited, but were ineligible because they were non-English speaking (*n*=7) or had notbeen homeless within the last 3 months (*n*=4). The prevalence of MRSA nasal colonization among study participants was 8.3 %, based on isolates recovered in culture (*n*=16) (Table 2). Seventy-five per cent (*n*=12) of recovered MRSA isolates had clonal similarity to USA300, while 19 % of isolates (*n*=3) were identified as USA100 and 6.3 % (*n*=1) as USA500. Eighty-one per cent (*n*=13) of isolates were resistant to erythromycin, and levofloxacin resistance was identified in 31 % (*n*=5) of isolates. Inducible clindamycin resistance was identified in 23 % (*n*=3) of isolates. One isolate, a USA500 strain, expressed resistance to trimethoprim/sulfamethoxazole. All isolates were susceptible to tetracycline and vancomycin. Fifteen of 16 MRSA isolates (93.8 %) were resistant to at least 1 additional antibiotic in addition to oxacillin and penicillin (resistance to the latter is descriptive for MRSA categorization). One USA300 and one USA100 isolate were resistant to two antibiotics in addition to oxacillin and penicillin (erythromycin and clindamycin).

RISK FACTORS FOR MRSA NASAL COLONIZATION

Of the medical risk factors, currently undergoing haemodialysis for renal failure [OR: 12.6 (95 % CI: 1.6, 96.1); *P*=0.02] and a history of physician-diagnosed endocarditis [OR: 6.2 (95 % CI: 1.0, 36.7); *P*=0.05] were positively associated with MRSA nasal colonization. Being an inpatient in the hospital in the last 6 months was associated with a marginal, but non-significant, increase in MRSA nasal colonization risk [OR: 2.8 (95 % CI: 0.9, 8.3); *P*=0.07]. No association was observed between MRSA nasal colonization and recent antibiotic use, frequency of medical care, skin infection in the prior 6 months, recent use of the ED, or HIV infection.

In regard to behavioural factors, heavy drinking (defined as drinking to intoxication five or more times per week [34]) was positively associated with MRSA nasal colonization [OR: 5.2 (95 % CI 1.8, 15.4); *P*=0.003] (Table 3). Daily showering was associated with a 70 % reduction in the odds of MRSA nasal colonization [OR: 0.3 (95 % CI: 0.1, 0.8); *P*=0.01]. Likewise, increased transience in location of sleep, defined as sleeping in more than one location in the last week, was associated with a 40 % increase in the odds of MRSA nasal colonization [OR: 1.4 (95 % CI: 1.0, 1.8);

Table 1. Selected demographic data for study participants (*n*=194)

Characteristic	Prevalence % (n)
Gender	
Female	54.0 (105)
Male	43.5 (84)
Transgender female	1.6 (5)
Transgender male	0.5 (1)
Race/ethnicity	
Black	41.8 (81)
White	38.1 (74)
Hispanic	18.6 (36)
Educational attainment	
Less than high school	31.4 (61)
High-school graduate or GED	40.4 (78)
Place where individual slept most frequently in the last week	
Shelter	53.6 (104)
Street	7.2 (14)
Supportive or transitional housing	11.3 (22)
With a friend or family member	13.9 (27)
Housing without support services	8.8 (17)
Other	5.2 (10)
Self-reported medical history	
Symptoms of skin or soft tissue infection in the last 6 months*	36.6 (71)
Ever diagnosed with MRSA	16.0 (31)
HIV-positive	11.3 (22)
Ever diagnosed with endocarditis	3.1 (6)
Currently on haemodialysis for renal failure	2.1 (4)
Sought medical care in the emergency department in the last 6 months	64.4 (123)
Inpatient in the last 6 months	46.3 (88)
Behaviours and experiences	
Injection drug use in last year	27.8 (54)
Incarcerated in last year	16.0 (31)
Current smoker	80.9 (157)
Heavy drinker†	15.5 (30)
Recent antibiotic use	
Last 3 months	25.5 (49)
Last 6 months	44.3 (86)

*Includes symptom-based descriptions of abscesses, boils, cellulitis and folliculitis, as well as positive response to 'Have you had a skin infection in the last 6 months?' and 'Do you have a skin infection right now?'
†Defined as drinking to intoxication 5+ days in the last month.

Table 2. MRSA nasal colonization, antimicrobial resistance and strain type (*n*=16)

	Prevalence % (n)
MRSA nasal colonization	8.3 (16)
MRSA antibiotic resistance (*n*=16)	
Erythromycin	81.2 (13)
Levofloxacin	31.2 (5)
Clindamycin (inducible)	23.1 (6)
Trimethoprim/sulfamethoxazole	6.2 (1)
Vancomycin	0 (0)
Tetracycline	0 (0)
MRSA strain•	
USA100	18.8 (3)
USA300	75.0 (12)
USA500	6.3 (1)
USA300 antibiotic resistance (*n*=12)	
Erythromycin	75.0 (9)
Levofloxacin	16.7 (2)
Clindamycin (inducible)	8.3 (1)
Vancomycin	0 (0)
Tetracycline	0 (0)
Trimethoprim/sulfamethoxazole	0 (0)

*Circulating strain with greatest clonal similarity as generated using pulse-field gel electrophoresis (PFGE) at the Massachusetts State Public Health Laboratory (William A. Hinton State Laboratory Institute).

the National Health and Nutrition Examination Survey (NHANES) 2003–2004 data [35]. Our finding is similar to the nasal colonization prevalence identified in a recent study of homeless persons in Kansas City (9.8 %) [13].

Injection drug use is believed to increase susceptibility to *S. aureus* infections, particularly within skin and soft tissue. This is likely due to repeated breaks in the skin that introduce opportunities for *S. aureus* to enter the body, use of pathogen-contaminated injection equipment, immunosuppression mediated by drug use and comorbidities associated with addiction [27]. Approximately one-quarter of our study participants reported using injection drugs in the last year, although we did not observe elevated prevalence of MRSA nasal colonization among these individuals compared to persons who did not report drug use. Prior studies of injection drug users, for which there is often great overlap with homelessness in urban settings, reflect notably higher prevalence of MRSA nasal colonization compared to what we observed in this study [27, 36, 37]. This contrast may reflect differences in sample size and laboratory techniques (PCR versus culture), as well as population-specific differences in risk factors, such as incarceration, HIV status or underreporting of drug use.

Similarly, we did not observe elevated prevalence of nasal colonization among persons who had been incarcerated recently, although such findings have been observed in prior studies [38–41]. Surface contamination, crowded living

P=0.04]. No associations were seen between recent injection drug use, smoking status, or other behavioural or demographic factors.

Our findings indicate that homeless individuals in Boston experience a higher prevalence of nasal colonization of MRSA compared to estimates for the general population, the latter of which is estimated at approximately 1.5 % from

Table 3. Selected risk factors for MRSA nasal colonization among persons experiencing homelessness in Boston (*n*=194)

Risk factor	Odds ratio (95 % CI); *P*-value*
Inpatient in hospital in last 6 months	2.8 (0.9, 8.3); *P*=0.07
Currently on haemodialysis	12.6 (1.6, 96.1); *P*=0.02
Heavy drinking†	5.2 (1.8, 15.4); *P*=0.003
Daily showering	0.3 (0.1, 0.8); *P*=0.01
Increased night-time transience‡	1.4 (1.0, 1.8); *P*=0.04
Physician-diagnosed endocarditis	6.2 (1.0, 36.7); *P*=0.05

*Results from univariate logistic regression models. Results did not differ significantly in models adjusting for age and gender.
†Defined as drinking to intoxication five or more times per month.
‡Increase in MRSA nasal colonization risk associated with sleeping in >1 location in the last week.

conditions and reduced access to hygiene and medical care are hypothesized to increase *S. aureus* transmission and infection among persons who are incarcerated [42]. Approximately 16 % of study participants reported incarceration in the last year. It is feasible that the time frame of our questioning regarding incarceration (within 1 year) may have been too long to capture the risk of MRSA nasal colonization among these individuals.

Antibiotic-resistant pathogens pose specific concerns in treating homeless patients due to low rates of follow-up care and, as a result, population-wide data can inform treatment options. Notably, we observed that nearly 90 % of USA300 isolates were susceptible to clindamycin and two-thirds were susceptible to erythromycin, suggesting that these medications may be a feasible empirical treatment in this population; further study and local antibiogram data would provide more assurance for this choice. Low-level resistance to trimethoprim/sulfamethoxazole (Bactrim), a common first-line oral treatment for community-acquired MRSA, among USA300 isolates also reinforces the efficacy of this treatment option in this population.

The risk profile of individuals in this community who carry multi-drug resistant MRSA clones primarily associated with healthcare-associated infections are complex and may involve multiple risk factors for infection, including HIV infection, injection drug use, alcoholism and other comorbidities. The healthcare-associated USA500 strain was recovered from one patient, a 60 year-old man who reported intermittent homelessness since the age of 35, was HIV-positive and currently on haemodialysis for renal failure. Of the three participants colonized with USA100, which is also considered to be a healthcare-associated strain, all had been seen in the ED and two had been admitted as inpatients during the last 6 months. One patient was HIV-positive, on haemodialysis and reported a prior MRSA diagnosis, while a second patient reported a history of endocarditis. Two of these three patients reported injection drug use in the last year and heavy drinking in the last 30 days. Nasal colonization with clones associated with more severe clinical

outcomes, such as USA100 and USA500, increases the risk of poor outcomes for these individuals.

USA300 is the predominant community-acquired MRSA clone currently circulating in the United States [43]. USA300 dominated colonization among persons who reported sleeping outdoors the night before the study (100 % of colonization identified among persons who sleep on the street was USA300, compared to 70 % of persons who were sheltered). It is feasible that USA300 is more easily transmitted in the context of the limited access to sanitation facilities experienced by unsheltered individuals. Persons who slept on the street were significantly less likely to report taking a daily shower compared to sheltered persons (*P*=0.008) and were more likely to be transient (*P*=0.06), both of which were associated with MRSA nasal colonization in this study. The risk factors involving sanitation and hygiene in this population warrant further study with larger sample sizes.

Current haemodialysis treatment, heavy drinking and endocarditis emerged as significant risk factors for MRSA nasal colonization among people experiencing homelessness in this study. Due to the low numbers of individuals reporting haemodialysis and endocarditis, the confidence intervals are wide and the results should be interpreted with caution. Nevertheless, these findings reinforce those from previous studies of MRSA colonization risk factors among housed individuals [44, 45]. Heavy drinking was particularly associated with colonization of the community-acquired USA300.

While symptoms of SSTIs in the last 6 months were reported by more than one-third of study participants, we did not observe a significant relationship between recent or current SSTI and MRSA nasal colonization, which differs from the findings of prior studies [46, 47]. We did identify a more than twofold increase in the odds of MRSA nasal colonization among persons who reported a current skin infection, as well as consistently elevated odds of colonization among persons reporting abscesses, blisters, cellulitis and folliculitis in the last 6 months; however, these findings were not significant at the 0.05 % level. It is possible that the small sample size prevented the identification of significant findings between MRSA nasal colonization and SSTIs, or that a different bacterium, and not MRSA, was responsible for the SSTIs experienced by study participants.

Our study is limited by its small sample size, which poses a particular limitation in evaluating comorbid risk factors. The cross-sectional design did not allow us to link current colonization to later clinical outcomes. The use of culture and not PCR for MRSA detection may have resulted in misclassification; however, chromogenic media have been demonstrated to have higher MRSA specificity and sensitivity compared to PCR analyses following appropriate incubation steps [48]. Without culture, the additional strain typing data could not have been feasibly obtained and the cost of direct testing and sequencing was prohibitive for a small study. The analysis of a single body site to identify MRSA

colonization likely resulted in an underestimation of overall MRSA colonization, but was conducted to increase participant acceptance and reduce cost. Our study was also limited in not assessing multiple types of illicit drug use; we did not evaluate non-injectable drug use as a risk factor for MRSA infection in this population, which may be an important gap. The comparison to NHANES prevalence data is imperfect due to differences in age distribution between our study and the NHANES sample, the latter of which includes children. At a population level, MRSA prevalence is higher among older persons, which may be responsible for our elevated prevalence finding [35]. Despite these limitations, our study conducted in-person interviews and sampling among a highly vulnerable, hard-to-reach population and gained insights that may guide treatment and future intervention strategies for urban disadvantaged populations.

Future studies could consider environmental surface contamination with MRSA in shelters, specifically in bathrooms and sleeping facilities, and transmission networks among persons who sleep on the street. Decontamination studies in public sanitation facilities would be valuable to assess the effectiveness of environmental interventions. Targeted decolonization of homeless persons at high risk of MRSA infection, notably those on haemodialysis, may reduce infection risk. Additionally, specific interventions to improve access to and utilization of sanitation facilities among persons who are homeless and transient may address the elevated risk in these populations for sanitation-related infections, including MRSA.

Conflicts of interest
The authors declare that there are no conflicts of interest.

Ethical statement
All study materials and protocol were approved by the Boston University Medical Center IRB (H-33761).

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