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Major article

Prevalence and risk factors for methicillin-resistant *Staphylococcus aureus* in an HIV-positive cohort

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Background: Persons living with HIV (PLWH) are disproportionately burdened with methicillin-resistant *Staphylococcus aureus* (MRSA). Our objective was to evaluate prevalence and risks for MRSA colonization in PLWH.

Methods: Adults were recruited from Johns Hopkins University AIDS Service in Baltimore, Maryland. A risk questionnaire and specimen collection from anatomic sites with culture susceptibility and genotyping were completed. Generalized estimating equation modeling identified MRSA colonization risk factors.

Results: Of 500 participants, most were black (69%), on antiretroviral therapy (ART) (87%), with undetectable viral loads (73.4%). Median CD4 count was 487 cells/mm^3 (interquartile range, 316-676.5 cells/mm^3). MRSA prevalence was 15.4%, predominantly from the nares (59.7%). Forty percent were nares negative but were colonized elsewhere. Lower odds for colonization were associated with recent sexual activity (adjusted odds ratio [AOR] = 0.84, $P < .001$) and ART (AOR = 0.85, $P = .011$). Increased odds were associated with lower income (<$25,000 vs >$75,000; AOR = 2.68, $P < .001$), recent hospitalization (AOR = 1.54, $P < .001$), incarceration (AOR = 1.55, $P < .001$), use of street drugs (AOR = 1.43, $P < .001$), and skin abscess (AOR = 1.19, $P < .001$).

Conclusions: Even with high MRSA prevalence, the proportion identified through nares surveillance alone was low, indicating the importance of screening multiple anatomic sites. Associations were not found with same-sex coupling or black race. MRSA prevention might be a benefit of ART in PLWH.

Methicillin-resistant *Staphylococcus aureus* (MRSA) continues to cause excess morbidity and mortality among persons living with HIV (PLWH). In the United States, PLWH have substantially higher incidence of MRSA infections than the general population (12.3/1,000 person years compared with 1-2/1,000 person years),[1] and MRSA remains a substantial reason for hospital admission.[2] Metropolitan areas throughout the country have documented a substantial increase in MRSA infections,[3-5] peaking in 2008, with an incidence 5 times greater in PLWH than HIV-uninfected persons within a large health care system.[6] Despite recent reported declines in skin and soft tissue infection, PLWH continue to shoulder a disproportionate burden of disease.[7]

Key risk factors for MRSA colonization and infection have been identified as a result of these data and include substance abuse[8,9]; high-risk sexual practices in persons with greater numbers of sex partners, regardless of sexual orientation[10]; and having a sexual partner with a known skin infection.[10] Additional risks for MRSA infection among PLWH include male sex,[7] incarceration history,[7] lower CD4 counts,[4,5,10] high viral load,[4,11] recent hospital admission,[12] β-lactam antibiotic use,[3] lack of

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cotrimoxazole prophylaxis,[5,11] and known MRSA infection in the last 12 months.[3]

Despite recent attention to this issue, many questions related to the HIV-MRSA interface remain unanswered. To further understand risk and enable the improvement of this population's health and well-being and limit the spread of MRSA within and among partners, this study assessed the overall prevalence of MRSA colonization at multiple body sites among PLWH and their primary partners. In addition, we determined the risk factors that are associated with MRSA colonization.

METHODS

Study setting and participant selection

To assess colonization prevalence among PLWH, we conducted a cross-sectional epidemiologic evaluation of MRSA among persons within the Johns Hopkins University AIDS Service (JHUAS). The JHUAS is a hospital-based practice that provides specialty care at the Moore Clinic on the Johns Hopkins Hospital campus in downtown Baltimore, Maryland, and at Green Spring Station (GSS) in Baltimore County. Urban Baltimore has a high incidence of HIV infection and MRSA colonization within outpatient populations.[13,14] Greater than 50% of our clients reside in East Baltimore and >75% are within the city limits. The Moore Clinic follows an average of 2,000 clients annually, including the uninsured, with most residing in Baltimore City. Most are black (77%), with major HIV transmission risks of intravenous drug use and heterosexual sex. Colocated services include viral hepatitis clinic, counseling, case management, social work, laboratory services, wound care, and an outpatient pharmacy. The GSS medical office serves a smaller patient cohort ($n = 650$) that is primarily white (64%), with a greater proportion residing in Baltimore's surrounding counties. The major HIV transmission risk at GSS is men who have sex with men. The GSS Clinic also provides services to persons without HIV infection and does not accept the uninsured. There is an onsite laboratory and outpatient pharmacy. Many providers work at both the GSS and Moore Clinic locations.

Sample size calculations were informed by previous work showing a strong association between MRSA and previous or current abscess[15] along with community prevalence data for Baltimore City. Based on the projected probability of MRSA among persons with abscess (0.30) and the probability of abscess in the entire cohort (0.18), a sample size of 500 was needed to obtain 90% power at $\alpha = 0.05$ for a 2-tailed test. This sample size would allow us to detect associations between having a current abscess and MRSA colonization.

Subjects were recruited from March 1, 2010-June 30, 2010, with microbiologic analysis completed in April 2011. Eligible primary subjects were adult men and women ages ≥18 years with the ability to read or understand spoken English who receive care within the JHUAS. Potential participants were approached and screened consecutively during the recruitment period: every tenth patient entering the Moore Clinic and all patients at GSS. We gathered specimens from sexual partners to examine similarities and differences between partners and MRSA colonization. Sexual partners were eligible for inclusion if referred by the index HIV-positive subject, regardless of the partner's HIV status. Participants were offered a $25 gift card for participation. The study was approved by the Johns Hopkins Medicine Institutional Review Board.

Collection of clinical specimens

A total of 6 swabs for men and 7 for women were collected, plus an additional swab for anyone with a wound. Anterior nares, axillary, throat, groin, perineum, and rectal swabs were obtained using BactiSwab II dual-headed culturettes (Remel, Lenexa, KS). The perineum is the area between the anus and scrotum or vulva. Vaginal swabs were collected on both women and postoperative transgendered women. Wound specimens were obtained from any patient presenting with an open or draining wound. Two trained registered nurses collected all patient swabs. All swabs were collected during the clinic visit at study enrollment, transported at room temperature, and stored at 5°C until processing within 24 hours of collection.

Risk factor evaluation

A survey instrument was designed with a set of questions used in a questionnaire previously implemented within the same population to assess factors related to a person's hospital and community risks for MRSA acquisition. Another 13 questions were added to assess behavioral risk factors, leading to a 64-item questionnaire. The current study did not evaluate all 64 items. A study team member administered the questionnaire face-to-face during the clinic visit at study enrollment. Interviewers were trained in sexual history taking and pilot tested the survey instrument. Interviews were conducted in a private setting, and confidentiality of responses was ensured to address the tendency for subjects to provide socially desirable responses. Both clinic populations are routinely screened for sexually history and sexually transmitted infections at each clinic visit. The time frame for any sexual activity or drug use was the 12 months prior to the interview. Medical records were reviewed by research nurses for clarity of HIV-related or sexual history, comorbidities, admission data, and other self-reported information from the questionnaire. Information from medical records was used if discrepancies occurred with self-reported information.

Microbiologic evaluation

Using standard culture methods, a swab was streaked onto CHROMagar MRSA (BD Diagnostics, Sparks, MD) [CHROM-MRSA], a selective medium, and then placed in Trypticase soy broth with 6.5% NaCl. Gram-positive cocci that were catalase positive and latex agglutination positive were identified presumptively as *S aureus*. The presumptive *S aureus* isolates recovered from the enrichment broth were subbed and sent to the BD Phoenix Automated Microbiology System (BD Diagnostics, Sparks, MD)[16] for identification and susceptibility testing when the matching CHROM-MRSA agar plates were negative. All isolates growing on CHROM-MRSA were considered MRSA.

Staphylococcal genotyping was performed using the Ibis Staphylococcus Typing and Characterization kit (Ibis Biosciences, Carlsbad, CA). This multiplex, broad-based, molecular assay, performed in a microtiter plate format, uses primer sets that are capable of identifying *S aureus* (*tufB* and *nuc*) and distinguishing MSSA from MRSA (*mecA*). It also incorporates primers that determine the presence of Panton-Valentine leukocidin genes (LukS and LukD), toxic shock toxin 1 (TSST1), and high-level (*mupA*) and low-level (*ileS*) mupirocin resistance. Strain characterization is performed by multilocus sequence typing using a unique set of sequences from 7 common housekeeping genes for *S aureus*. The assay is based on the principle of polymerase chain reaction (PCR)—electrospray ionization mass spectrometry (ESI-MS) and is performed on the Ibis T5000 instrument (Ibis Biosciences, Carlsbad, CA).[17,18] The assay was performed according to the manufacturer's instructions and interpreted according to the guidelines in the reference by Wolk et al.[18]