

# *Staphylococcus epidermidis* Protection Against *Staphylococcus aureus* Colonization in People Living With Human Immunodeficiency Virus in an Inner-City Outpatient Population: A Cross-Sectional Study

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**Background.** People living with human immunodeficiency virus (PLWH) have been disproportionately affected by methicillin-resistant *Staphylococcus aureus* (MRSA) colonization and infection, in particular by clones USA300 and USA500. However, the contribution of epidemiological, bacterial, and immunological risk factors to the excess of *S aureus* in PLWH remain incompletely understood.

**Methods.** In this cross-sectional study, we determined the prevalence and molecular epidemiology of *S aureus* colonization in 93 PLWH attending an urban human immunodeficiency virus (HIV) clinic. Participants completed a structured interview assessing demographic information and risk factors for MRSA. Swabs were obtained from the nose, throat, and groin and cultured for *S aureus* and *Staphylococcus epidermidis*.

**Results.** Most participants had well controlled HIV infection (89, 96% CD4 >200). Thirty-six (39%) individuals were colonized with *S aureus* at 1 or more body sites, including 6 (6%) with MRSA. Regular gym use was a risk factor for *S aureus* but not MRSA carriage. In contrast, *S epidermidis* was present in almost all individuals (n = 84, 90%), predominantly in the nares (n = 66, 71%). Using generalized estimating equation models, we observed that the odds of *S aureus* colonization were significantly and drastically reduced when *S epidermidis* was detected ( $P = .0001$ ). After controlling for site, gender, and age, we identified that the odds of *S aureus* colonization were 80% less if *S epidermidis* was present (adjusted odds ratio, 0.20; 95% confidence interval, .09–.45;  $P < .0001$ ).

**Conclusions.** Taken together, we observed a lower prevalence of *S aureus* and MRSA colonization than has been previously reported in PLWH. In this cohort, colonization with *S epidermidis* was protective against *S aureus* colonization.

**Keywords.** HIV; immune dysregulation; MRSA; *Staphylococcus aureus*; *Staphylococcus epidermidis*.

Over the past 15 years, community-associated methicillin-resistant *Staphylococcus aureus* infections (CA-MRSA) have emerged sequential to healthcare-associated (HA) MRSA infections [1]. Community-associated MRSA account for the majority of skin and soft tissue infections (SSTIs) in the United States [2]. People living with human immunodeficiency virus (PLWH) have been disproportionately affected by both HA- and CA-MRSA as evidenced by their increased frequency of *S aureus* colonization, skin infections, and invasive blood stream infections [3–6]. Some studies have suggested that PLWH have a 6–18 times higher incident rate of *S aureus* infection when compared with healthy human immunodeficiency virus (HIV)-negative controls [3, 7].

The increased incidence of *S aureus* infections is likely multifactorial and includes behavioral, host immune, and pathogen factors [5, 7]. It has been shown that injection drug use, homelessness, high-risk sexual activity, or extended hospital stays can contribute to this increased burden [8, 9]. Moreover, severe immunodeficiency as manifested by low CD4 counts significantly contribute to worse *S aureus* outcomes [10], but even in PLWH on antiretroviral therapy the overall incidence of *S aureus* colonization and disease remains significantly elevated [5, 11].

In the healthcare setting, nasal carriage of MRSA has been associated with subsequent MRSA infections [12]. The role of *S aureus* and MRSA colonization in subsequent infections is less clear in the community setting [13]. More recently, colonization of body sites other than the nares have been recognized as potential reservoirs for infecting *S aureus* strains [14, 15], including in PLWH [6]. These studies have also suggested that certain clonal types such as USA300 and USA500 preferentially colonize certain body sites such as the groin, in particular in patients infected with HIV [16, 17]. This suggests possible specific interactions between the impaired immune system after HIV infection and the molecular make-up of distinct *S aureus*

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clones. Patients with HIV infection, even when on antiretroviral therapy, appear to have persistent defects in Th17-mediated immune responses, which are critical in controlling *S aureus* infections [18, 19]. Moreover, concomitant increased Th2 response and chronic immune activation can lead to the downregulation of antimicrobial peptides human  $\beta$ -defensin (hBD)2 and hBD3, which are also important in the keratinocyte response to *S aureus* [20].

In addition to host factors, *S aureus* colonization is also determined by interaction with local microbiota. It has been suggested that the frequent commensal *Staphylococcus epidermidis* in particular has the ability to directly inhibit *S aureus* colonization by secretion of a serine protease, Esp1, or by activation of Toll-like receptor-2 on keratinocytes, triggering the release of antimicrobial peptides [20, 21]. The importance of this interaction in patients with HIV remains unknown.

In this study, we aimed to determine the prevalence and molecular epidemiology of *S aureus*, MRSA, and *S epidermidis* colonization in an inner-city population of HIV-infected individuals.

## METHODS

### Study Population

This cross-sectional study was reviewed and approved by the Columbia University Medical Center (New York, NY) Institutional Review Board. The study took place in January and February 2013 at the New York Presbyterian's Comprehensive HIV Program clinic. Patients were informed about the study by their primary care provider and, after giving verbal consent to be contacted, were approached by the study team. After providing written informed consent, patients were recruited into the study. In total, 96 patients met the inclusion criteria of being HIV positive and  $\geq 18$  years of age; 93 patients completed the survey and provided all body site swabs. Patients attending the clinic were ineligible to participate if their HIV status was negative or unknown ( $n = 1$ ); or if they had inflammatory bowel disease ( $n = 1$ ). Other predefined exclusion criteria of active or acute acquired immune deficiency syndrome-defining opportunistic infections within 4 weeks before study entry or the current use of systemic immunosuppressive medications (eg, corticosteroids) within 14 days before study entry were not encountered. Participants were compensated with a \$10 gift card to a CVS Pharmacy.

### Survey

Patients completed structured interviews using audio computer-assisted self-interviewing software. Questions assessed demographic information and risk factors for MRSA, including personal care habits, as well as pertinent aspects of medical, social, and sexual histories. In addition, retrospective reviews of patient medical records were undertaken to ascertain relevant clinical and laboratory information. This also included

assessment of underlying skin diseases (eczema, psoriasis, seborrheic dermatitis, lichenoid dermatitis, skin allergies, acne, tinea, basal cell carcinoma, and zoster) or skin and soft tissue infections and opportunistic infections and antibiotic exposures over the 3 months before enrollment.

### Microbiological Sample Collection and Molecular Studies

After completing the survey, the nose, throat, and groin of participants were sampled using sterile premoistened swabs (BD BBL CultureSwab; BD Diagnostic Systems, Sparks, MD). Additional skin sites were sampled if study participants reported possible infected skin lesions. Samples were processed as previously described [22]. In brief, culture swabs were incubated overnight at 37°C in 6% salt-supplemented Tryptic soy broth and plated onto Mannitol salt agar (Becton Dickinson, Sparks, MD). Positive, mannitol-fermenting yellow colonies were isolated onto 5% sheep blood/Tryptic soy agar plates (blood/TSA) (Becton Dickinson). *Staphylococcus aureus* was identified from blood/TSA by coagulase and Protein A detection kit (Murex StaphAurex). In addition, all nonmannitol-fermenting and Staphaurex-negative colonies were isolated onto TSA (Becton Dickinson, Sparks, MD). *Staphylococcus epidermidis* was identified from TSA by species-specific polymerase chain reaction (PCR) as previously described [23].

All *S aureus* isolates were genotyped by staphylococcal protein A (*spa*) repeat-region sequencing and analysis (Ridom-staphsoftware). Strain relatedness was further evaluated using integrated based-upon repeat pattern (BURP) algorithms for *spa* Clonal Complex clustering (*spa*-CCs) [22]. Presence and type of Staphylococcal Chromosomal Cassette (SCC)*mec*, determined by multiplex PCR, was used to evaluate methicillin resistance [24]. Isolates were further genotyped by testing for the presence of the arginine-catabolic mobile element (ACME) gene by PCR [22].

All *S epidermidis* isolates were tested for the presence of the serine protease *esp* gene by PCR [21]. For antibiotic susceptibility testing, we randomly selected 1 *S epidermidis* isolate per participant from half of the *S epidermidis*-colonized individuals, due to cost restraints. Isolates were tested for resistance to penicillin, levofloxacin, gentamicin, erythromycin, linezolid, tetracycline, cefoxitin, and rifampin using the Kirby-Bauer method and Clinical and Laboratory Standards Institute (CLSI) standards [25].

### Statistical Analyses

All statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC). We tested 2 separate outcomes against each hypothesized risk factor: colonization with *S aureus* (methicillin-sensitive *S aureus* [MSSA] or MRSA) at any body site or colonization with MRSA at any body site. Comparisons of colonized to noncolonized participants on dichotomous variables were carried out using  $\chi^2$  or Fisher's exact tests where appropriate. Bivariate analyses with continuous predictors were evaluated using unpaired Student *t* tests. Generalized

estimating equations (GEEs) were used to evaluate the relationship between *S aureus* and *S epidermidis* colonization. This method allowed us to control for the multiple body site swabs taken per individual. All statistical tests were 2-sided, with  $P < .05$  considered significant.

## RESULTS

### Study Demographics and Colonization Prevalence

This cross-sectional study included 93 HIV-positive participants with a mean age of 50 (interquartile range, 44–60). Approximately one third of the population was female ( $n = 32$ , 34%), two thirds were male ( $n = 60$ , 65%), and 1 individual was transgender ( $n = 1$ , 1%; [Table 1](#)). Hispanics ( $n = 44$ , 48%) and African Americans ( $n = 34$ , 37%) comprised the largest ethnic groups in our study, whereas whites ( $n = 9$ , 10%) and other races ( $n = 5$ , 5%) were less frequently represented. The majority of participants self-identified as heterosexual ( $n = 55$ , 59%); one third ( $n = 31$ , 33%) self-identified as men who have sex with men (50% of men). Most participants had well controlled HIV infection because 89 individuals (96%) had a recent CD4 count  $>200$  and an undetectable viral load at their most recent visit. Only 4 patients had a recent viral load  $>1000$ . Few participants ( $n = 5$ , 5%) were hospitalized in the 3 months preceding study participation.

The self-reported burden of prior *S aureus* infections was low. Approximately one fifth ( $n = 20$ , 22%) of the study population reported ever having been diagnosed with an *S aureus* infection, and very few of these infections ( $n = 3$ , 3%) had occurred within the past year. Eleven participants (12%) had a skin infection in the past 3 months. Twenty-two participants reported using antibiotics within 3 months before study participation, which was confirmed for 20 patients by clinical chart review. Other common risk factors for *S aureus* infections, such as receiving tattoos ( $n = 3$ ), recent incarceration ( $n = 1$ ), or injection drug use ( $n = 1$ ), were infrequently reported.

By culturing the nares, throat, and groin, we identified 36 individuals colonized with *S aureus* at 1 or more body sites (39%). Of these, 6 were colonized with MRSA (6%). Colonization with *S aureus* was most prevalent at the nares ( $n = 28$ , 30%), followed by throat ( $n = 16$ , 17%), groin ( $n = 11$ , 12%), and other sites ( $n = 2$ , 2%). Colonization occurred at multiple sites in 14 individuals, including 5 with colonization at all 3 sites. Eight individuals were colonized only at the throat or groin without concomitant nasal colonization ([Figure 1A](#)).

We detected *S epidermidis* colonization in a majority of individuals at 1 or more body sites ( $n = 84$ , 90%). Colonization with *S epidermidis* was most prevalent at the nares ( $n = 66$ , 71%), followed by throat ( $n = 50$ , 54%), groin ( $n = 37$ , 40%), and other sites ( $n = 11$ , 12%). Nearly two thirds of *S epidermidis* colonized individuals were colonized at multiple body sites ( $n = 53$ , 57%); 18 were colonized at all 3 sites. Colonization with any *S aureus*, MRSA alone, or *S epidermidis* at each body site did not differ between males and females ([Table 2](#)).

### Molecular and Phenotypic Characterization

Among the 36 colonized individuals, we observed 26 different *spa*-types. Of the 14 individuals colonized at multiple body sites, only 1 had different *spa*-types at the 3 tested body sites. The vast majority of colonizing isolates were MSSA (86%) and belonged to a diversity of *spa*-types ([Figure 1B](#)). The most frequent *spa*-type was t002, accounting for 15% of MSSA isolates. Half of the MRSA isolates were *spa*-type t008, consistent with USA300. Six of the 8 MRSA isolates (75%) were ACME positive, consistent with USA300. We observed *spa*-type t064 in both the MSSA and MRSA group.

*Staphylococcus epidermidis* have been associated with substantial antibiotic resistance [26]. Antibiotic susceptibility testing on a subset of the *S epidermidis* collection showed that nearly all isolates were resistant to penicillin ( $n = 40$ , 93%; [Figure 2](#)). Only 12% ( $n = 5$ ) were resistant to cefoxitin, consistent with methicillin-resistant *S epidermidis* ([Figure 2](#)). Methicillin-resistant *S epidermidis* strains were more likely to be nonsusceptible to tetracycline compared with the methicillin-sensitive *S epidermidis* group (80% vs 13%, respectively; Fisher's exact test,  $P = .005$ ). The 2 groups had no other significant differences in antibiotic susceptibilities, and all isolates were susceptible to linezolid, rifampin, and vancomycin. All *S epidermidis* isolates were typed for the *esp* gene and were positive.

### Risk Factors for *Staphylococcus aureus* Colonization

To assess for risk factors of *S aureus* colonization, we carried out bivariate analyses. Participants colonized with *S aureus* at any body site were more likely to have regularly used a gym within the last 3 months (44%) compared with those who were not colonized (21%;  $P = .019$ ; [Table 1](#)). However, this association did not hold for carriage of MRSA ( $P = .067$ ). A reported history of *S aureus* infections within 1 year of the interview was not associated with carriage of *S aureus* or MRSA. No other demographic characteristics or healthcare risk factors were significantly different when comparing carriers to noncarriers.

Almost all participants (90%) were colonized with *S epidermidis* at 1 or more body sites. The *esp* gene was ubiquitous throughout this sample collection, with all isolates displaying positive PCR results. On the individual level, we found that 5 of the 6 (83%) MRSA-colonized individuals and 27 of the 30 (90%) MSSA-colonized individuals were also colonized with *S epidermidis* at at least 1 body site. However, collapsing the data onto the individual level does not take into account variation across body sites. Hence, we chose to further investigate this relationship by stratifying our observations by swabbed body site. We found that when the nose or throat was colonized with *S epidermidis*, *S aureus* colonization was less likely to co-occur at the same site. This was most apparent in the throat, where only 2 participants were cocolonized, compared with 14 who were colonized with *S aureus* alone ([Table 3](#)).

**Table 1. Demographics, HIV History, and *Staphylococcus aureus* Risk Factors of the Study Population**

Characteristic	Total N (%)	<i>S aureus</i> Colonization			MRSA Colonization		
		Yes (N = 36)	No (N = 57)	<i>P</i> <sup>a</sup>	Yes (N = 6)	No (N = 87)	<i>P</i> <sup>a</sup>
<b>Demographics</b>							
Gender (n = 92)							
Male	60 (65)	25	35	.21	5	55	.68
Female	32 (34)	11	21		1	31	
Ethnicity (n = 92)							
Hispanic	44 (48)	18	26	.36	2	42	.09
African American	34 (37)	10	24		1	33	
White	9 (10)	5	4		2	7	
Other	5 (5)	3	2		1	4	
Residence							
Apartment/house	81 (87)	32	49	.76	6	75	1
Other <sup>b</sup>	12 (13)	4	8		0	12	
Sexual orientation							
MSM	31 (33)	11	20	.65	3	28	.40
Other	62 (67)	25	37		3	59	
Work							
Unemployed	55 (59)	21	34	.083	2	53	.12
Employed	31 (33)	13	18		3	28	
Retired	5 (5)	0	5		0	5	
Student	2 (2)	2	0		1	1	
Mean age (SD)	50 (11)	51 (11)	50 (12)	.55	47 (12)	50 (12)	.51
<b>HIV History</b>							
HIV risk factor (n = 89)							
Sex (male-female)	44 (49)	19	25	.94	3	41	.90
Sex (male-male)	30 (34)	11	19		3	27	
Healthcare-associated	7 (8)	2	5		0	7	
Multiple risks	6 (7)	2	4		0	6	
Injection drug use	2 (2)	1	1		0	2	
Current CD4 count							
<200	4 (4)	2	2	.94	1	3	.07
200 to 500	31 (33)	12	19		0	31	
≥500	58 (62)	22	36		5	53	
Mean current CD4 % (SD) (n = 92)	28 (10)	27 (10)	28 (11)	.69	31 (8)	27 (11)	.38
CD4 nadir (n = 89)							
<100	29 (33)	12	17	.78	2	27	1
≥100	60 (67)	23	37		4	56	
Current* viral load							
Nondetectable	69 (74)	28	41	.14	4	65	.71
20–1000	20 (22)	5	15		2	18	
>1000	4 (4)	3	1		0	4	
<b><i>S aureus</i> risk factors</b>							
Lives with <5-year-olds	2 (2)	1	1	1	0	2	1
Lives with a pet	36 (39)	14	22	.98	3	33	.67
Lives alone	39 (42)	18	21	.21	3	36	.39
Uses a gym* (n = 92)	28 (30)	16	12	.019	4	24	.07
Shares towels	6 (6)	4	2	.20	0	6	1
Shares clothes	2 (2)	1	1	1	0	2	1
Shaving, any site	85 (91)	33	52	1	4	81	.08
<b><i>S aureus</i> infections</b>							
Ever	20 (22)	9	11	.51	2	18	.61
MSSA	12 (13)	3	9	.36	0	12	1
MRSA	8 (9)	6	2	.052	2	6	.08
Within 1 year	3 (3)	2	1	.56	1	2	.18
MSSA	2 (2)	1	1	1	0	2	1
MRSA	1 (1)	1	0	.39	1	0	.06

**Table 1. Continued**

Characteristic	Total N (%)	<i>S aureus</i> Colonization			MRSA Colonization		
		Yes (N = 36)	No (N = 57)	<i>P</i> <sup>a</sup>	Yes (N = 6)	No (N = 87)	<i>P</i> <sup>a</sup>
History of skin condition	24 (26)	10	14	.73	2	22	.65
Previous skin infections							
Ever	15 (16)	4	11	.35	0	15	.58
Recent*	11 (12)	4	7	1	0	11	1
Any sexual partners* (n = 89)	49 (55)	16	33	.097	4	2	.69
Sexual partner with skin wounds	2 (2)	1	1	1	0	2	1
Hospital admission* (n = 92)	5 (5)	0	5	.15	0	5	1
Past opportunistic infections							
Any	25 (27)	8	17	.42	0	25	.19
Thrush	15 (16)	4	11	.30	0	15	.58
PCP	8 (9)	2	6	.48	0	8	1
Kaposi's sarcoma	3 (3)	0	3	.28	0	3	1
Antimicrobial exposure*							
Trimethoprim-sulfamethoxazole	7 (8)	2	5	.70	0	7	1
Mupirocin	2 (2)	1	1	1	0	2	1
Dapsone	3 (3)	1	2	1	0	3	1
Other antimicrobials	10 (11)	3	7	.74	0	10	1

Abbreviations: HIV, human immunodeficiency virus; MSM, men whom have sex with men; MRSA, methicillin-resistant *S aureus*; MSSA, methicillin-sensitive *S aureus*; PCP, pneumocystis pneumonia; SD, standard deviation; SRO, single-room occupancy.

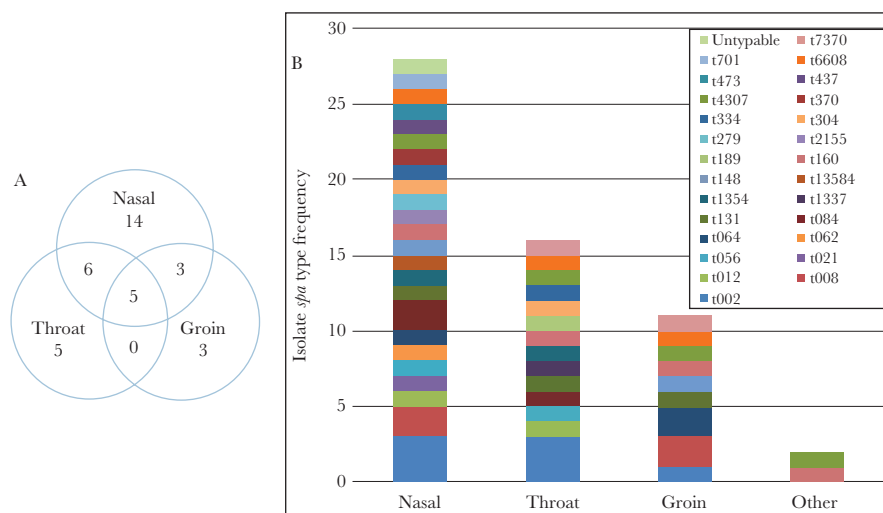
\*Variable was assessed for the 3 months preceding study enrollment.

<sup>a</sup> $\chi^2$  or Fisher's exact test was used for analyses of dichotomous variables. Unpaired Student *t* test was used for analyses of continuous variables.

<sup>b</sup>SROs, transitional, and shelters.

Because swabs from the same individual cannot be considered independent observations, we used GEE models to assess the statistical significance of *S epidermidis* colonization on *S aureus* colonization. In the GEE model, an interaction term between body site and *S epidermidis* colonization was not significant. We found that the odds of *S aureus* colonization were significantly and drastically reduced when *S epidermidis* was detected ( $P = .0001$ ; Table 3). After controlling for swab

site, gender, and age, we identified that the odds of *S aureus* colonization were 80% less if a person was colonized with *S epidermidis* (adjusted odds ratio [aOR], 0.20; 95% confidence interval, .09–.45;  $P < .0001$ ) (Table 3). More importantly, this dramatic protective effect did not differ significantly across body sites (interaction term nonsignificant;  $P = .10$ ). We were unable to perform a similar analysis on MRSA alone due to low numbers.



**Figure 1.** *Staphylococcus aureus* colonization (A) by body site and (B) by frequency of *spa* types, stratified on body site. Data are expressed as absolute frequencies. Genotyping of isolates from all body sites yielded 26 unique *spa*-types.

**Table 2. *Staphylococcus aureus* and *Staphylococcus epidermidis* Colonization Prevalence by Body Site and Gender**

	<i>S aureus</i>			MRSA			<i>S epidermidis</i> (esp-Positive)		
	Male	Female	P <sup>a</sup>	Male	Female	P <sup>a</sup>	Male	Female	P <sup>a</sup>
N = 92*									
Nasal	19	9	.73	3	0	.55	41	24	.50
Throat	12	4	.37	2	0	.54	36	13	.08
Inguinal	7	4	1	2	1	1	23	13	.83

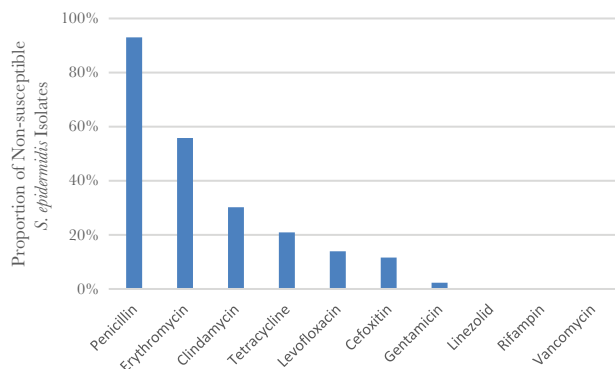
Abbreviations: MRSA, methicillin-resistant *S aureus*.

\*Transgender individuals were excluded.

<sup>a</sup>χ<sup>2</sup> or Fisher's exact test was used for analyses.

## DISCUSSION

In this population of HIV-positive individuals attending an urban comprehensive HIV clinic, we observed a lower prevalence of MRSA colonization (6.5%) compared with 15%–20% reported in previous studies on individuals infected with HIV [6, 27]. However, the prevalence of MRSA colonization was still higher than the 1.5% reported nationally from the general population [28] and what we previously observed in healthy individuals attending the hospital's dental clinic (2%) [22]. Moreover, the overall prevalence of *S aureus* colonization by 3 body-site screening (39%) was relatively low compared with prior studies in other HIV study populations [29]. More importantly, GEE aOR indicated a protective effect of *S epidermidis* against *S aureus* colonization. It appears unlikely that this effect was mediated by Esp1 protease because all *S epidermidis* isolates carried the corresponding gene. It has been suggested that this enzyme harbors direct activity against *S aureus* [21], although Fredheim et al [30] also found no association between presence of the *esp* gene and *S aureus* carriage. These differences might reflect clonal variability of *S aureus* isolates between studies and *S aureus* resistance to Esp-mediated killing in some samples. Although USA300 and USA500 were predominant amongst



**Figure 2. *Staphylococcus epidermidis* antibiograms.** Susceptibilities were determined using the Kirby-Bauer disk diffusion method and compared against Clinical and Laboratory Standards Institute standards.

**Table 3. GEE Models Assessing the Association of *Staphylococcus epidermidis* With *Staphylococcus aureus* Colonization**

SA Colonization (MSSA or MRSA)	SE Colonized	Not SE Colonized
Nasal	N = 66	N = 27
SA colonized	11 (17)	17 (63)
Not SA colonized	55 (83)	10 (37)
Throat	N = 50	N = 43
SA colonized	2 (4)	14 (33)
Not SA colonized	48 (96)	29 (67)
Inguinal	N = 37	N = 56
SA colonized	5 (14)	6 (11)
Not SA colonized	32 (86)	50 (89)
Variables in GEE Model	OR of SA Colonization (95% CI)	SE Parameter PValue
SE	0.32 (0.18–0.57)	.0001
SE, site*	0.20 (0.09–0.44)	<.0001
SE, site, gender, age	0.20 (0.09–0.45)	<.0001

Abbreviations: CI, confidence interval; CLSI, Clinical and Laboratory Standards Institute; GEE, generalized estimating equation; MRSA, methicillin-resistant *S aureus*; MSSA, methicillin-sensitive *S aureus*; OR, odds ratio; SA, *S aureus*; SE, *S epidermidis*.

\*Swab site was not a significant effect measure modifier of the association between SE and SA colonization.

MRSA isolates consistent with prior studies [16, 17], MSSA were highly diverse in our study population.

Alternative means of *S epidermidis* conferring protection to *S aureus* might involve other direct bacterial effectors such as the release of phenol soluble modulins, lantibiotics, or an indirect effect via modulating the local immune response. This includes *S epidermidis*-mediated induction of interleukin (IL)-17A(+) CD8(+) T cells that migrate to the epidermis and skin [31]. It has been shown that clearance of nasal *S aureus* carriage requires T cells and IL-17A, which leads to recruitment of neutrophils. Even after initiation of antiretroviral treatment and recovery of CD4 cells, the T-cell homeostasis in infected patients remains disturbed and includes a Th2 polarization away from Th-17, upregulation of regulatory T cells, and persistently elevated CD8 T cell counts. Future studies are needed to address how polarization of the T-cell response in HIV patients contributes to colonization with *S aureus* and *S epidermidis* and potential competition between these organisms.

Competition between *S aureus* and *S epidermidis* is likely not restricted to PLWH [31] and might also differ at particular sites. Few studies have assessed the prevalence of *S epidermidis* colonization in healthy individuals [32]. Our observations here are comparable to early investigations where colonization ranged from 62% at the legs and 78% at the nares to 92% in the axillae [33, 34]. More recently, *Staphylococcus lugdunensis* has been suggested as capable of inhibiting *S aureus* colonization at the nares via release of lugdunin [35]. A series of investigations has also documented the contribution of the innate immune response to mediate competition between bacteria such as *Haemophilus influenzae* and *Streptococcus pneumoniae* at mucosal sites [36].

In a recent meta-analysis of 6558 PLWH from 32 studies, 6.9% were MRSA carriers. A history of hospitalization over the past year conferred a 3.1 times higher risk and recent incarceration a 1.7 times higher risk of MRSA colonization [37]. Several important differences between our study and others need to be considered. High-risk social behaviors such as drug use or recent incarceration as well as crowding were low in our study population as were previous *S aureus* infections or recent hospital admission [38, 39]. Our patient population was slightly older with an average age of 50 [5, 27], and we enrolled a higher proportion of heterosexual men and overall more women (34%) than others [5, 27, 39, 40]. The majority of our study population was Hispanic, which has previously been associated with lower MRSA colonization in PLWH [27]. Although we did not observe significant gender differences between *S aureus* carriage in the current study, we recently observed that men attending a sexually transmitted disease clinic were almost 4 times more likely to harbor *S aureus* in the anterior nares [15]. Gym use was significantly associated with *S aureus* colonization ( $P = .019$ ), but it was not associated with MRSA colonization ( $P = .067$ ), which might be explained by our relatively small sample size. In a recent study, Crum-Cianflone et al [38] also identified public gym use as a risk factor for *S aureus* colonization and concluded that specific behaviors, rather than HIV-related risk factors, predicted *S aureus* colonization and SSTIs.

Low CD4 counts (<100) have been associated with an increased risk of MRSA colonization in previous studies from approximately 10 years ago [41–43]. Participants in our study were under better control and, on average, had high CD4 counts. Although approximately one third of participants had a documented CD4 nadir of <100, CD4 nadir was not associated with MRSA or *S aureus* colonization. Antibiotic exposure over the past 3 months was overall low (~20%) compared with other studies in this community (~50%) [22], despite the use of prophylactic antibiotics to prevent opportunistic infections, and might have contributed to the lower MRSA prevalence. Antibiotic resistance in *S epidermidis* was also low.

Several limitations to our study need to be considered. This was a relatively small sample, with low MRSA prevalence and surveyed over a short time period. The study might have lacked power to detect small differences between colonized and noncolonized individuals. The study population reflects a single clinic in an urban environment with low self-reported behavioral risk factors for *S aureus* carriage. We did not measure immune markers such as soluble CD14 or IL-17 and their potential impact on *S aureus* colonization. We used standard culture techniques for isolation of *S aureus* [22]. We cannot exclude that this approach may have interfered with isolation of *S epidermidis*. However, given the high prevalence of *S epidermidis* colonization at the different body sites, this appears less likely.

## CONCLUSIONS

Taken together, our results of a relatively low MRSA prevalence likely reflect a combination of PLWH with well controlled HIV and lack of high-risk behaviors previously associated with *S aureus* colonization and infection. Further research should explore whether the observed protective effect of *S epidermidis* on *S aureus* colonization extends beyond PLWH and what the molecular mediators of these interactions are.

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