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Anatomic Sites of Colonization with Community-Associated Methicillin-Resistant *Staphylococcus aureus*

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Methicillin-resistant *Staphylococcus aureus* (MRSA) has emerged over the past 20 years as a cause of infections in community populations, so-called community-associated MRSA (CA-MRSA). By pulsed-field gel electrophoresis (PFGE) subtyping, USA300 is the most common CA-MRSA strain in the US. It has been suggested that the colonization dynamics for CA-MRSA may be different than those for traditional MRSA strains[1], with extra-nasal colonization potentially playing a role in CA-MRSA transmission and infection[1].

Another distinguishing characteristic of USA300 MRSA strains is greater susceptibility to non-β-lactam antibiotics compared to healthcare-associated MRSA strains. However, multi-drug resistant (MDR) USA300 strains have been described, largely among HIV-infected patients and men who have sex with men (MSM)[2]. Also of concern, resistance to common decolonizing agents such as mupirocin[2] and chlorhexidine gluconate (CHG)[3] has been reported in CA-MRSA.

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The objectives of this study were to examine the phenotype of USA300 MRSA strains, the prevalence of the *qac*A/B gene in this population, and the anatomic sites of colonization by PFGE pattern.

We previously reported on the prevalence of nasal and extra-nasal CA-MRSA colonization among inpatients (374 HIV-infected and 371 HIV-negative) at Stroger Hospital of Cook County (CCH), the major safety-net hospital in Chicago, IL[4]. As described elsewhere, nasal and extra-nasal (throat, axilla, inguinal, peri-rectal, and chronic wound if present) surveillance swab specimens were collected from patients within 72 hours of admission from March 2011-April 2012; cultures were processed with broth enrichment[4]. Gender was recorded and enrolled men were asked if they identified themselves as MSM. Genotypic analysis with PFGE was performed on all identified MRSA isolates. Results were interpreted as described by McDougal, et al[5].

Confirmed MRSA isolates had antibiotic susceptibility determined (MicroScan Walkaway System, Siemens Healthcare Diagnostics, West Sacramento, CA). For USA300 MRSA strains, MDR was defined as resistance to four or more non-β lactam antibiotic classes. High-level mupirocin resistance was assessed using disk diffusion[6].

Carriage of *qac*A and *qac*B genes, which code for efflux pumps associated with increased minimum inhibitory concentrations (MICs) of CHG[7], was assessed using real-time PCR as described previously[8].

Chi-square analysis was used to examine the association of PFGE patterns and colonization sites, with Fisher's exact test used for small samples. SAS software version 9.2 (SAS Institute, Cary, NC) was used for statistical analysis. The study was approved by the Institutional Review Board of CCH and Rush University Medical Center.

We observed that following the nares, the peri-rectal area was the second most common site of colonization (58% of colonized individuals). Prevalence of extra-nasal and exclusive extra-nasal colonization was not significantly different between patients colonized with USA300 or non-USA300 strains (Table 1). However, the average number of sites colonized was significantly higher for USA300 versus non-USA300 strains [2.8 (SD 1.51) and 2.2 (1.48), respectively, p=0.049]. Inguinal, peri-rectal, and concomitant inguinal and peri-rectal colonization were all significantly associated with colonization with the USA300 strain type in comparison to non-USA300 MRSA strains (Table 1). Inguinal or peri-rectal MRSA colonization was found more often in men (63/480; 13%)—MSM (OR=2.2; 95% CI, 1.1, 4.2; p=0.02) and heterosexual men (OR=1.8; 95% CI, 1.02, 3.2; p=.04)—than in women (20/265; 8%), OR=1.9 (95% CI, 1.1, 3.1), p=0.02.

There were 5 individuals who had a MRSA infection at the time of enrollment and they were all found to have colonization with MRSA. Four of these individuals had SSTIs and were colonized with the USA300 strain type and one individual had a bloodstream infection and was colonized with a non-USA300 strain type. Excluding chronic wound cultures, each of these individuals had 3–5 sites of MRSA colonization, suggesting a significant level of extra-nasal colonization and colonization burden for individuals infected with MRSA.

3.4% of colonized individuals carried high-level mupirocin-resistant strains (1 USA100, 2 USA500, 1 USA300). Of the individuals colonized with USA300 MRSA strains, 4 (5%) carried MDR strains. There were 117 MRSA isolates evaluated for the presence of the *qac*A/B genes; all were negative.

We examined colonization and molecular characteristics of CA-MRSA isolates collected from patients seeking care at the major safety-net hospital in Chicago. We found that inguinal and peri-rectal colonization was more common with the USA300 strain type than with non-USA300 MRSA strains. In addition, highly antibiotic resistant USA300 MRSA strains were rare and none of the MRSA isolates collected over a 14 month study period was found to harbor the *qac*A/B genes.

We observed that males—both heterosexual males and MSM—had a higher prevalence of inguinal and peri-rectal MRSA colonization in comparison to females. Similarities observed in colonization patterns between MSM and heterosexual males suggest that perhaps social, hormonal, skin biology, or genetic differences between genders play a role in colonization dynamics rather than sexual orientation[9].

The absence of *qac*A/B genes among MRSA isolates in the population we studied is consistent with other reports in the US[10]. In contrast to reports in San Francisco[2], MDR USA300 strains were relatively rare in our population, which comprised a diverse group of HIV-infected and HIV-negative individuals. However, continued surveillance of antibiotic resistance patterns is needed to understand the evolving epidemiology of USA300 strains as well as to inform empiric therapeutic decisions.

Our study is limited in that we did not assess frequency of mupirocin or CHG use in our population, although CCH does not have mupirocin on its antibiotic formulary and CHG bathing use has been limited to ICU and pre-operative patients. In addition, we relied on self-report of MSM status which could lead to recall bias. Finally, we performed PFGE on one MRSA colony morphotype per body site and therefore may have failed to detect coexistent minority subpopulations.

In summary, our study highlights that inguinal and peri-rectal colonization appears to be more frequent with the USA300 strain type and that gender may play a role in location of extra-nasal CA-MRSA colonization. Patients with clinical MRSA infections appeared to be those with more sites of MRSA colonization. Although mupirocin resistance and presence of *qac*A/B were uncommon, continued monitoring of MRSA prevalence and resistance is warranted.

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Table 1

Association of Pattern of Anatomic Site of Colonization and Pulsed-Field Gel Electrophoresis Profile among Individuals Colonized with Community-Associated Methicillin-Resistant *Staphylococcus aureus*

	USA300[a](n=79)	non-USA300 (n=36)	OR (95% CI)	p value
Anatomic Site of Colonization				
Anterior nares	50 (63%)	21 (58%)	--	0.61
Throat	35 (44%)	16 (44%)	--	0.99
Axilla	31 (39%)	12 (33%)	--	0.54
Inguinal	49 (62%)	15 (42%)	2.3 (1.02, 5.11)	0.04
Peri-rectal	52 (66%)	15 (42%)	2.7 (1.2, 6.06)	0.015
Inguinal and peri-rectal region	40 (51%)	9 (25%)	3.1 (1.28, 7.37)	0.01
Wound	6 (8%)	1 (3%)	--	0.43
Extra-nasal colonization	74 (94%)	32 (89%)	--	0.46
Exclusive extra-nasal colonization	29 (37%)	15 (42%)	--	0.61
Average number of sites colonized (SD)	2.8 (1.51)	2.2 (1.48)	--	0.049

Data are No. (%) of patients, unless otherwise indicated.

NOTE. Any extra-nasal colonization was defined as the presence of CA-MRSA extra-nasal colonization irrespective of anterior nares culture results. Exclusive extra-nasal colonization was defined as CA-MRSA colonization at extra-nasal sites and negative anterior nares cultures for CA-MRSA.

[a] Two individuals were colonized with both USA300 and non-USA300 strains and were excluded from the comparison of USA300 to non-USA300 strains. Therefore, the total number of patients used in the analysis was 115.