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Original Article

Burden of perianal *Staphylococcus aureus* colonization in nursing home residents increases transmission to healthcare worker gowns and gloves

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Abstract

Objective: To evaluate the effect of the burden of *Staphylococcus aureus* colonization of nursing home residents on the risk of *S. aureus* transmission to healthcare worker (HCW) gowns and gloves.

Design: Multicenter prospective cohort study.

Setting and participants: Residents and HCWs from 13 community-based nursing homes in Maryland and Michigan.

Methods: Residents were cultured for *S. aureus* at the anterior nares and perianal skin. The *S. aureus* burden was estimated by quantitative polymerase chain reaction detecting the *nuc* gene. HCWs wore gowns and gloves during usual care activities; gowns and gloves were swabbed and then cultured for the presence of *S. aureus*.

Results: In total, 403 residents were enrolled; 169 were colonized with methicillin-resistant *S. aureus* (MRSA) or methicillin-sensitive *S. aureus* (MSSA) and comprised the study population; 232 were not colonized and thus were excluded from this analysis; and 2 were withdrawn prior to being swabbed. After multivariable analysis, perianal colonization with *S. aureus* conferred the greatest odds for transmission to HCW gowns and gloves, and the odds increased with increasing burden of colonization: adjusted odds ratio (aOR), 2.1 (95% CI, 1.3–3.5) for low-level colonization and aOR 5.2 (95% CI, 3.1–8.7) for high level colonization.

Conclusions: Among nursing home patients colonized with *S. aureus*, the risk of transmission to HCW gowns and gloves was greater from those colonized with greater quantities of *S. aureus* on the perianal skin. Our findings inform future infection control practices for both MRSA and MSSA in nursing homes.

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Staphylococcus aureus is an important cause of healthcare-associated infections. *S. aureus* is transmitted through direct or indirect contact with a colonized or infected person, and healthcare workers (HCWs) often serve as the vector for *S. aureus* transmission. Because of concerns about worse outcomes and limited treatment options, infection prevention practices are typically more aggressive for methicillin-resistant *S. aureus* (MRSA) than for methicillin-sensitive *S. aureus* (MSSA).[1,2] As a result, contact precautions are used for patients colonized with MRSA to prevent transmission to other patients, while standard precautions are typically used for patients colonized with MSSA. However, both MRSA and MSSA have similarly severe clinical manifestations. Despite increasing interest, a limited number of studies of *S. aureus* transmission include MSSA to justify this difference in infection prevention strategies.[3]

The risk factors for *S. aureus* transmission are multifactorial and are under active investigation.[4] Although it seems intuitive that the burden of colonization would also confer a greater risk of transmission, only a few studies have quantified MRSA colonization, and even fewer have assessed MSSA colonization or the relationship between colonization burden and transmission.[1,5,6] Herein, we examine the risk factors for *S. aureus* transmission—including both MRSA and MSSA—from community-based nursing home residents to HCW gowns and gloves to assess whether the risk of transmission is higher with a greater burden of colonization.

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Methods

Study design

We conducted a multicenter, prospective cohort study to estimate the frequency of and risk factors for *S. aureus* transmission to gowns and gloves worn by HCWs when providing care to nursing home residents as previously reported.[4] The protocol was approved by the institutional review boards of the University of Maryland Baltimore and University of Michigan.

Population

We screened 2,148 nursing home residents, of whom 695 were ineligible: 425 were not expected to stay >1 week from enrollment, 201 were identified by nursing home staff as being combative or having behavioral problems, and 69 did not speak English. Of the 1,453 eligible residents, 1,050 were not enrolled: 564 did not consent, 176 their legally authorized representative did not respond, and 310 were not approached about the study. The remaining 403 residents were enrolled from 13 community-based nursing homes in Maryland and Michigan. Residents were included in this study if they were colonized with *S. aureus* upon enrollment, as determined by swab culture from the anterior nares or perianal skin. However, 232 were not colonized and thus excluded from this analysis, and 2 were withdrawn prior to being swabbed, yielding our cohort of 169 *S. aureus*–colonized residents.

Data collection

We recorded clinical data about the residents obtained from the minimum data set, medical records, and nursing home personnel.[7] The HCWs were asked to wear gowns and gloves immediately prior to interacting with residents for up to 28 days after resident enrollment. Each interaction was comprised of 1 or more usual care activities (eg, toileting, then bathing, then dressing). A research coordinator observed and recorded the type of care activities delivered during each interaction. After the interaction, the coordinator swabbed the HCW's gown and gloves, as described previously.[8–10]

Laboratory procedures

Specimens from residents, gowns, and gloves were cultured for *S. aureus* at a central laboratory as previously described.[4] *Staphylococcus aureus* DNA was extracted from medium inculcated with resident swabs. Bacterial cells were lysed with lysostaphin (cat. no. L7386-15MG; Sigma-Aldrich, St Louis, MO) at a final concentration of 200 μg/mL at 37°C for 1 hour. The DNA was then purified from bacterial cell lysate with the Qiagen DNeasy Blood and Tissue Kit (Qiagen, Hilden, Germany). Quantitative polymerase chain reaction (qPCR) targeting the *nuc* gene was performed on those swabs that grew *S. aureus* with the iQ5 Real Time Detection System, iQ Supermix (Bio-Rad Laboratories, Hercules, CA). The *nuc* gene is present as a single copy in almost all *S. aureus*, but not other bacteria, and thus should correlate with colony-forming units (CFU) of *S. aureus*. It is a common molecular target for the rapid detection of *S. aureus* in blood and food samples and can be used to determine *S. aureus* colonization status.[11–13] In *in vitro* validation of our q-PCR methods, the number of *nuc* gene copies isolated from serial dilutions of standard MSSA (ATCC 43300) and MRSA (ATCC 29213) isolates (American Type Culture Collection, Manassas, VA) correlated well across a range of 10^3–10^7 CFU with the quantitative cultures of these isolates ($r = 0.997$ and 0.999, respectively).

Each *S. aureus* isolate was typed by DNA sequencing analysis of a single locus, the protein A (*spa*) gene hypervariable region as previously described.[14] Alleles were identified based on comparison to the sequences in the database at http://spaserver.ridom.de/. The *spa* types were grouped for each table by multilocus sequence type and were divided into each of 4 main groups: (1) t002 and those related to sequence type 5, (2) t008 and those related to sequence type 8, (3) t1081, and (4) other.

Statistical analysis

We defined the outcome of *S. aureus* transmission between a resident and HCW as the recovery of *S. aureus* isolates with matching methicillin susceptibility profiles from the patient (ie, colonization of the anterior nares or perianal skin) and the HCW (ie, the gown or glove worn during an interaction with a resident). The risk of *S. aureus* transmission for each resident was estimated as a fraction: the number of interactions resulting in *S. aureus* transmission divided by the total number of interactions. We did not analyze specific care activities because of small sample sizes and bundling within the same interaction (eg, toileting, then bathing, then dressing). We also reasoned that resident characteristics might correlate with specific types of care (eg, residents with wounds receive wound care). Residents were divided into the following 3 groups defined by the percentage of interactions resulting in transmission of *S. aureus*: (1) no transmission (0% of interactions), (2) low transmission (1%–30% of interactions), and (3) high transmission (>30% of interactions). The mean qPCR values from the perianal skin were divided into 3 categories of *S. aureus* colonization: (1) no colonization (0 CFU), (2) low burden of colonization (1–100 CFU), and (3) high burden of colonization (>100 CFU). The low- and high-colonization burden groups were compared to the no-colonization group as a reference. The mean qPCR values from the anterior nares were categorized as low burden of colonization (0–1,000 CFU) and high (>1,000 CFU) burden of colonization; 1,000 CFU was the lower limit of persistent nasal colonization described by Nouwen et al.[15] A series of the Pearson χ^2 tests for trend (for categorical data) or Kruskal-Wallis tests (for continuous variables) examined the association of transmission with a single independent variable. Odds ratios for transmission—dichotomized into transmission versus no transmission groups—were determined for those categorical variables with a $P < .20$.

The final multivariable model included risk factors with the odds ratios that were statistically significant: male sex, the presence of diabetes, pressure ulcer, indwelling urinary catheter, total dependence for transfer, residential care, burden of *S. aureus* colonization of the perianal skin by qPCR, and MRSA colonization. *S. aureus* colonization burden of the anterior nares by qPCR, while not statistically significant, was included in the multivariable model because of biological plausibility. The multivariable logistic regression (SAS proc GENMOD, employing a logit link, and binomial distribution) produced adjusted odds ratios for each of the independent variables in the model. The generalized estimating equations method (GEE) of Liang and Zeger, with an exchangeable covariance structure, was used to account for serial auto-correction of repeat measures from the same subjects.[16] All analyses were performed with and without outliers as identified by Cook's distance. Statistical tests were 2-tailed, and P values <0.05 were considered statistically significant. Statistical analyses were conducted using

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Stata version 15 software (StataCorp, College Station, TX) and SAS version 9.3 software (SAS Institute, Cary, NC).

Results

Gown and glove cultures were collected from 1,418 total interactions from the 169 subjects colonized with *S. aureus* in the anterior nares or perianal skin; 37% of the residents were male and 75% were non-Hispanic white. Table 1 lists resident groups by their risk of transmitting to gowns or gloves (eg, the high transmission group transmitted *S. aureus* to gowns or gloves in >30% of the care interactions). Residents in the high-transmission group were more likely to be male, to be diabetic, to have a pressure ulcer, to have *S. aureus* colonization at the perianal skin, to have a relatively high burden of *S. aureus* colonization at the perianal skin, or to be colonized with MRSA. q-PCR values were significantly greater in the high-transmitter group for both the anterior nares and perianal skin. We did not find an association between high *S. aureus* transmission and *spa* type, though a novel *spa* type t1081 was noted in 16 isolates. The association between *S. aureus* transmission and antibiotic use at enrollment, total dependence on a HCW for transfer, residential care, and acute-care hospitalization in the past 3 months were likewise not statistically significant.

The bivariate and multivariable analyses included 168 subjects and 1,417 interactions, with a median cluster size of 7 interactions per subject (range, 1–22); 1 subject and 1 interaction were excluded because of missing data. In the bivariate analysis, the odds of transmission increased >2-fold if the patient was male, had diabetes, had an indwelling urinary catheter, was totally dependent on a HCW for transfer, had perirectal colonization with *S. aureus*, or had MRSA colonization (Table 2). The odds of transmission increased markedly with increasing burden of perirectal colonization. The bivariate odds were also increased if the subject had a pressure ulcer or was in residential care. Neither antibiotic use at enrollment, nor a high burden of *S. aureus* in the anterior nares were significant risk factors.

In the multivariable analysis, colonization of the perianal skin had the greatest adjusted odds for *S. aureus* transmission, with increasing odds as the burden of colonization increased (Table 2). The multivariable odds ratios of transmission associated with being male, having diabetes, and having a urinary catheter were lower than the bivariate odds ratios but still statistically significant; the adjusted odds ratio of being in residential care remained unchanged. Having a pressure ulcer, being totally dependent on an HCW for transfer, and MRSA colonization were no longer statistically significant in the multivariable model. These odds ratios were unchanged when potential outliers were deleted based on Cook's distance.

Discussion

The transmission of *S. aureus* between a resident and a HCW is a key step in the spread of *S. aureus* in healthcare facilities, and it appears to be influenced by resident- and culture-based characteristics. In this study, nursing home residents with a high burden of perianal *S. aureus* colonization were more likely to transmit *S. aureus* to HCW gowns and gloves, and it is possible that some of the other risk factors for transmission share this common causal pathway.

The presence of *S. aureus* on the perianal skin conferred the greatest odds for *S. aureus* transmission to HCW gowns and gloves in the multivariable analysis. Here, the odds of *S. aureus* transmission increased with increasing burden of colonization, with the greatest odds ratio corresponding to those residents with >100 CFU from their perianal swab. Nasal carriers of *S. aureus* who are also perineal carriers have been reported to have higher *S. aureus* loads and disperse more *S. aureus*, which is consistent with our findings.[17–19] In contrast, a high burden of nasal colonization ($>10^3$ CFU) was not a significant risk factor in the multivariable model, which may reflect that HCWs are more likely to come in contact with other colonization sites (eg, axilla, groin, or perianal region).

Having a pressure ulcer and total dependence for transfer were not associated with *S. aureus* transmission after adjusting for perianal colonization burden, perhaps because these variables share a common pathway. Previous studies have linked perianal *S. aureus* colonization to *S. aureus*-specific lesions (eg, furuncles or carbuncles) of the lower half of the body,[20] and areas of skin breakdown, such as pressure ulcers, are often colonized with *S. aureus*.[21,22] Residents who are totally dependent for transfer are likely at increased risk for developing a pressure ulcer because of additional risk factors such as immobility or incontinence. Conversely, residents with pressure ulcers are more dependent on HCWs.

Diabetes and male sex remained significant risk factors for transmission after adjusting for perianal burden of colonization. Although diabetes has been linked to both nasal *S. aureus* colonization and perianal colonization burden, it is possible that diabetics could be colonized at additional sites outside of the nares or perineum and lead to greater transmission.[23,24] The link between being male and transmission is unclear, though higher levels of colonization have been attributed to hormonal differences.[25,26]

Being in residential care—rather than post-acute care—and the presence of a urinary catheter were also significant risk factors for transmission in the multivariable model. Patients in residential care may have greater care needs, which result in a higher cumulative exposure to their healthcare workers and facilities. Although *S. aureus* is not a typical urinary pathogen, an indwelling catheter provides a surface for colonization and a portal for infection, possibly via colocalization of *S. aureus* with fibrinogen,[27] which may be exacerbated by manipulation of the catheter by the resident or HCW. Moreover, the association between having an indwelling catheter and *S. aureus* colonization has been reported previously.[28]

MRSA colonization was not a significant risk factor after adjusting for confounders, likely because colonization with any *S. aureus*—and not necessarily just MRSA—is the driver of transmission risk. We did not observe a difference in the risk of transmission among residents colonized with different *spa* types, suggesting that the strain of *S. aureus* may not be a determining factor in transmission. We did note an unusual *spa* type t1081 as a common cause of perianal colonization, which has been reported as a common *spa* type in nursing homes and hospitals in both The Netherlands and Hong Kong.[29–34] Interestingly, *spa* type t1081 has also been associated with increased transmission[29,32] and patients in a bedbound state,[34] possibly due to its predilection for perianal colonization.

The strengths of this study include its prospective, multicenter design with representation from different parts of the nation. This was a community-based study with similar demographics to those of the US nursing home population with respect to gender and ethnicity.[35–37] Additionally, surveillance cultures were obtained at enrollment to document colonization, rather than using historical colonization data. Limitations include that gown and glove transmission is a surrogate outcome for the transmission of *S. aureus* from resident to HCW to another resident, though mechanistically reasonable to study in lieu of resident-to-resident

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Table 1. Characteristics of *Staphylococcus aureus*–Colonized Residents (n=169) Stratified by Level of Transmission to HCW Gowns and Gloves

Characteristic	No Transmission (0%) (n=58) No. (%)[a]	Low Transmission (1-30%) (n=48) No. (%)[a]	High Transmission (>30%) (n=63) No. (%)[a]	*P* Value[b]
Resident-based characteristics				
Age (median, IQR)	81 (71–86)	81 (71–85)	75 (66–87)	.26
Male	13 (22)	16 (33)	33 (52)	<.01
Diabetes	11 (19)	20 (42)	39 (62)	<.01
Skin breakdown				
Pressure ulcer[c]	5 (9)	7 (15)	16 (25)	.01
Surgical wound(s)	13 (22)	8 (17)	5 (8)	.03
Other	2 (3)	1 (2)	3 (5)	.69
Devices				
Indwelling urinary catheter	2 (3)	6 (13)	8 (13)	.09
Ostomy	3 (5)	3 (6)	2 (3)	.60
Feeding tube	5 (9)	1 (2)	3 (5)	.36
Antibiotic use at enrollment	2 (3)	5 (10)	8 (13)	.08
Total dependence for transfer	7 (12)	8 (17)	15 (24)	.09
Residential care	24 (41)	17 (35)	35 (56)	.11
Acute-care hospitalization, past 3 mo	35 (60)	28 (58)	37 (60)	.94
Culture-based Characteristics				
S. aureus colonization				
Anterior nares	57 (98)	44 (92)	61 (97)	.72
Perianal skin	4 (7)	9 (19)	39 (62)	<.01
S. aureus q-PCR, anterior nares, median (IQR)	103 (11–9,957)	270 (13–14,778)	1,491 (92–101,712)	.03
S. aureus q-PCR, anterior nares				.15
No/Low burden (0–1,000 CFU)	36 (62)	27 (56)	31 (49)	
High burden (>1,000 CFU)	22 (38)	21 (44)	32 (51)	
S. aureus q-PCR, perianal skin (median, IQR)	0 (0–0)	0 (0–0)	3 (0–363)	<.01
S. aureus q-PCR, perianal skin				<.01
No burden (0 CFU)	53 (93)	41 (85)	30 (48)	
Low burden (1–100 CFU)	3 (5)	6 (13)	13 (21)	
High burden (>100 CFU)	1 (2)	1 (2)	20 (32)	
MRSA colonization	30 (52)	34 (71)	47 (75)	<.01
spa types				
Anterior nares n=158[d]				
t002 & related	23 (42)	16 (38)	23 (38)	.78
t008 & related	8 (15)	8 (19)	13 (21)	
t1081	2 (4)	2 (5)	6 (9)	
Other	22 (40)	16 (38)	19 (31)	
Perianal skin n=52				
t002 & related	1 (25)	6 (67)	14 (36)	
t008 & related	1 (25)	3 (33)	6 (15)	.15
t1081	1 (25)	0 (0)	8 (21)	
Other	1 (25)	0 (0)	11 (28)	

Note. HCW, healthcare worker; SD, standard deviation; IQR, interquartile range; MRSA, methicillin-resistant *S. aureus.*
[a]Units unless otherwise specified.
[b]Comparing transmission groups.
[c]Stage 1 or worse.
[d]4 isolates were not typable.

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Table 2. Odds Ratios of *S. aureus* Transmission to HCW Gowns and Gloves Given Resident- and Culture-Based Characteristics Using GEE to Adjusting for Within-Resident Clustering

Characteristic	Bivariate Analysis (n=168)[a] OR (95% CI)	Multivariable Analysis (n=168)[a] Adjusted OR (95% CI)
Resident-based characteristics		
Male	2.33 (1.55–3.53)	1.57 (1.07–2.30)
Diabetes	2.18 (1.44–3.30)	1.98 (1.32–2.97)
Pressure ulcer	1.81 (1.12–2.93)	0.79 (0.47–1.35)
Indwelling urinary catheter	2.30 (1.30–4.39)	1.76 (1.04–3.00)
Antibiotic use at enrollment	1.45 (0.80, 2.63)	. . .
Total dependence for transfer	2.14 (1.24–3.72)	1.62 (0.95–2.75)
Residential care	1.65 (1.09–2.50)	1.75 (1.13–2.70)
Culture-based characteristics		
S. aureus q-PCR, anterior nares		
High burden (>1000 CFU)	1.18 (0.78–1.79)	1.28 (0.90–1.83)
S. aureus q-PCR, perianal skin		
Low burden (1–100 CFU)	2.95 (1.78–4.87)	2.11 (1.27–3.53)
High burden (>100 CFU)	6.03 (3.78–9.61)	5.20 (3.13–8.66)
MRSA colonization	2.36 (1.50–3.73)	1.41 (0.96–2.09)

Note. HCW, healthcare worker; GEE, generalized estimating equations; OR, odds ratio; CI, confidence interval; q-PCR, quantitative polymerase chain reaction; CFU, colony-forming units;
[a]1 resident was excluded because of missing data.

S. aureus acquisition, which is a relatively rare outcome. We could not adjust for repeated measurements of the same nursing home staff member because HCW participation was anonymous. Among 13 nursing homes, however, a variety of staff members were involved, and we used the GEE in our analysis to account for multiple interactions with the same resident. Selection bias toward those residents capable of providing informed consent might have affected our findings, though we engaged the legally authorized representatives of those who were unable to provide informed consent to obtain a representative sample.

In our study, we identified factors that promote *S. aureus* transmission to HCW gowns and gloves in nursing homes. We have shown that the burden of *S. aureus* colonization on the perianal skin is a marker for those most likely to transmit to HCW gowns and gloves. To our knowledge, this is the first study to relate the burden of colonization to the risk of transmission. Unlike most other studies, we examined all *S. aureus* transmission because both MRSA and MSSA are clinically important entities. Our results suggest that targeting MRSA-colonized residents alone may not be the optimal approach to controlling *S. aureus* transmission. Perianal skin colonization can be used to identify those residents who are most likely to transmit *S. aureus* to others, and who may warrant infection control interventions such as contact precautions or enhanced barrier precautions.[38] Future studies should assess whether decreasing the burden of perianal colonization, perhaps through enhanced hygiene, could decrease *S. aureus* transmission.

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Conflicts of interest. All authors report no conflicts of interest relevant to this article.

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