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Prevalence and correlates of MRSA and MSSA nasal carriage at a Ugandan regional referral hospital

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Background: Despite increasing antimicrobial resistance globally, data are lacking on prevalence and factors associated with *Staphylococcus aureus* (SA) and MRSA carriage in resource-limited settings.

Objectives: To determine the prevalence of SA and MRSA nasal carriage and factors associated with carriage among Ugandan regional referral hospital patients.

Methods: We enrolled a cross-section of 500 adults, sampling anterior nares for SA and MRSA carriage using Cepheid Xpert SA Nasal Complete.

Results: Mean age was 37 years; 321 (64%) were female and 166 (33%) were HIV infected. Overall, 316 (63%) reported risk factors for invasive SA infection; 368 (74%) reported current antibiotic use. SA was detected in 29% and MRSA in 2.8%. MRSA and MSSA carriers were less likely than SA non-carriers to be female (50% and 56% versus 68%, $P = 0.03$) or to have recently used β-lactam antibiotics (43% and 65% versus 73%, $P = 0.01$). MRSA carriers were more likely to have open wounds than MSSA carriers and SA non-carriers (71% versus 27% and 40%, $P = 0.001$) and contact with pigs (21% versus 2% and 6%, $P = 0.008$). MRSA carriage ranged from 0% of HIV clinic participants to 8% of inpatient surgical ward participants ($P = 0.01$). In multivariable logistic regression analysis, male sex was independently associated with SA carriage (OR 1.68, 95% CI 1.12–2.53, $P = 0.01$) and recent β-lactam antibiotic use was associated with reduced odds of SA carriage (OR 0.61, 95% CI 0.38–0.97, $P = 0.04$).

Conclusions: MRSA nasal carriage prevalence was low and associated with pig contact, open wounds and surgical ward admission, but not with HIV infection.

Introduction

Monitoring and limiting antibiotic resistance is a focal point for antibiotic stewardship and cost-containment programmes worldwide.[1] *Staphylococcus aureus* (SA) is one of the most common bacteria isolated clinically and can cause life-threatening infections. SA may acquire genetic mutations promoting resistance to commonly used first-line antibiotics and MRSA may emerge. Invasive MRSA infections may not be treatable by antimicrobials readily accessed in sub-Saharan Africa including penicillins and cephalosporins, though less serious infections may respond to clindamycin, doxycycline or trimethoprim/sulfamethoxazole, where available.

Multiple studies have reported the prevalence of SA carriage in high-resource areas, which may be increasing.[2] Risk factors for SA colonization in these settings include male sex, younger age, comorbid medical conditions, recent hospitalization and exposure to certain livestock.[3–5] In the USA, MRSA infections are associated with recent hospitalization[6] and MRSA colonization of the anterior nares,[7] though community-associated MRSA infections occur frequently. MSSA and MRSA carriers are more likely to develop invasive staphylococcal infections than non-carriers, including skin and soft tissue infections,[8] pneumonia,[9] bacteraemia[10] and orthopaedic hardware infections.[11] In resource-limited settings, the prevalence of MRSA is incompletely described,[12] and risk factors

associated with carriage and invasive infection may not be identical to high-resource areas.

To address this gap in knowledge, we enrolled a cross-sectional cohort of 500 Ugandan adults seeking care at a Ugandan regional referral hospital to survey for MSSA and MRSA carriage and determine factors associated with carriage in this setting.

Patients and methods

Ethics

The study was approved by the institutional ethics review boards at Mbarara University of Science and Technology (16-11/13), Partners Healthcare (2014P000638/MGH) and the Uganda National Council of Science and Technology (HS/1705).

Study population and clinical data collection

Participants were recruited from Mbarara Regional Referral Hospital (MRRH) in Mbarara, Uganda from February to September 2015. MRRH is a 300 bed academic teaching and referral hospital serving a predominantly rural, agrarian population. Patients were enrolled from the inpatient surgery, medicine and maternity wards, general outpatient department and outpatient HIV clinic. All patients ≥18 years of age receiving care at the respective ward or clinic were eligible and consecutive patients at each location were approached for enrolment until the target number of participants had been enrolled and enrolment was shifted to the next location. All participants provided written informed consent. Potential participants were excluded if they did not speak English or Runyankole, or were incapacitated and next-of-kin declined participation. Demographic characteristics, health conditions and antibiotic usage were determined using a structured face-to-face interview in English or Runyankole developed by study investigators.

Sample collection, processing and data entry

Both anterior nares of study participants were swabbed with sterile rayon-tipped dual swabs, which were placed in tubes containing Amies medium-soaked sponges, transported to the adjacent Epicentre Mbarara Research Centre laboratory and refrigerated. Within 24 h, one swab was tested using Cepheid Xpert SA Nasal Complete assay and interpreted according to the manufacturer's instructions. Commercially available MRSA ATCC 33591 and MSSA ATCC 25923 strains were run as positive controls. All invalid runs were repeated once. Questionnaires and results were recorded on paper and entered manually into a Research Electronic Data Capture (REDCap)[13] database.

Data analysis

We calculated a sample size of 500 based on an estimated 5% MRSA nasal carriage prevalence, to have 80% power to detect true carriage prevalence of 5% with a 95% confidence estimate precision of ∼5% ± 3%. Descriptive statistics were used to characterize the cohort. Differences in baseline characteristics between the three sub-groups (MRSA carriage, MSSA carriage, no SA carriage) were assessed using a χ^2 test, or Fisher's exact test for cell sizes <5. Characteristics were also compared between those with any SA carriage (combining MRSA and MSSA subtypes) and no SA carriage and between MRSA and MSSA carriage. Multivariable logistic regression was used to identify factors associated with the outcome of any SA carriage, including both MRSA and MSSA subtypes, similar to prior analyses.[14,15] SA carriage correlates with a $P < 0.1$ in univariable logistic regression analysis were included in the multivariable model. All variables in the final model with $P < 0.05$ were considered statistically significant independent predictors of the SA carriage outcome. The small number of MRSA carriers precluded separate multivariable analyses for that outcome. All analyses were performed using Stata software (Version 12.0; StataCorp, College Station, TX, USA).

Results

At each of five MRRH locations, 100 participants were enrolled with a total of 500 participants overall. Over 95% of patients approached for enrolment agreed to participate. Missing variables ranged from 0.2% (sex) to 1.8% (age). The mean age was 36.6 years (standard deviation 15.3, range 18–101). Females comprised 321 (64.3%) of the cohort. The most common co-morbidity was HIV and 166 (33.3%) of participants self-reported HIV infection. Overall 316 (63.3%) reported a known risk factor for invasive SA infection, including open wounds (188, 37.8%), rash (99, 19.8%), corticosteroid use within the last month (40, 8.0%), receipt of chemotherapy within the last year (4, 0.8%) or immune suppressing medication (24, 4.8%). Most participants (317, 63.4%) reported no previous hospitalization, 368 (73.6%) reported current antibiotic use and 350 (70.1%) reported β-lactam use within the last year (Table 1).

Of 500 samples, 499 yielded a valid GeneXpert result. Of these, 145 (29.1%) were positive for SA and 14 (2.8%) were positive for MRSA (9.7% of SA positives). MRSA and MSSA carriers were less likely than SA non-carriers to be female (50% and 56% versus 68%, respectively, $P = 0.03$) or report β-lactam antibiotic use within the last year (43% and 65% versus 73%, $P = 0.01$). MRSA carriers were more likely to have open wounds than MSSA carriers and SA non-carriers (71% versus 27% and 40%, respectively, $P = 0.001$) and live or work with pigs (21% versus 2% and 6%, $P = 0.008$). MSSA carriage was highest in the HIV clinic (35%) and lowest on the maternity ward (17%); MRSA carriage was highest on the surgical ward (8%) and lowest in the HIV clinic (0%) ($P = 0.001$). SA carriage was highest on the medical ward (36%) and lowest on the maternity ward (13%) ($P = 0.04$).

In multivariable logistic regression models, male sex was independently associated with SA carriage (OR 1.68, 95% CI 1.12–2.53, $P = 0.01$) and recent β-lactam antibiotic use was associated with reduced odds of SA carriage (OR 0.61, 95% CI 0.38–0.97, $P = 0.04$) (Table 2).

Discussion

In this cross-sectional study among predominantly rural-dwelling Ugandan inpatients and outpatients, we found moderate prevalence of SA carriage (29.1%) and low prevalence of MRSA carriage (2.8%, 9.7% of SA carriers). Our results are among the first from this region to describe SA nasal carriage prevalence and associated factors, and we report carriage prevalence similar to studies elsewhere.[2,16] These findings contribute data necessary to prevent, control and contain effectively the antibiotic-resistant pathogens such as MRSA in resource-limited settings.

In contrast to other studies, we found no association between MRSA nasal carriage and self-reported HIV status. MRSA carriage is thought to be more common among HIV-infected individuals, with a reported prevalence of 6.9% in a recent global meta-analysis,[17] though no data from Africa were included. SA carriage has been associated with other chronic diseases, immunosuppression and household member illness.[18] However,

Table 1. Characteristics of study participants and results of bivariate analysis of factors associated with nasal MSSA or MRSA colonization compared with no SA colonization; $N = 499$

Characteristic	Number (%) not SA colonized, $n = 354$	Number (%) MSSA colonized, $n = 131$	Number (%) MRSA colonized, $n = 14$	P^a
Age, years ($n = 490$)				0.53
18–25	99 (28)	30 (24)	2 (14)	
26–35	91 (26)	42 (33)	5 (36)	
36–45	83 (24)	28 (22)	3 (21)	
46–55	38 (11)	9 (7)	1 (7)	
>55	38 (11)	18 (14)	3 (21)	
Female sex ($n = 498$)	241 (68)	73 (56)	7 (50)	0.03
Resides in Mbarara district ($n = 496$)	168 (48)	59 (46)	7 (50)	0.92
Lives by self ($n = 498$)	45 (13)	18 (14)	3 (21)	0.63
Lives with >5 other people ($n = 498$)	113 (32)	39 (30)	7 (50)	0.30
HIV infected	109 (31)	53 (40)	4 (29)	0.13
Cancer diagnosis	22 (6)	11 (8)	3 (21)	0.08
Diabetes mellitus	15 (4)	0 (0)	0 (0)	0.04
Chronic illness, excluding HIV	76 (22)	34 (26)	6 (43)	0.13
Lives or works with pigs	21 (6)	3 (2)	3 (21)	0.008
Lives or works with dogs	33 (9)	7 (5)	3 (21)	0.09
Lives or works with cows	67 (19)	23 (18)	4 (29)	0.60
Has ≥1 open wounds	142 (40)	36 (27)	10 (71)	0.001
Has a rash	61 (17)	37 (28)	1 (7.1)	0.01
Uses tobacco ($n = 494$)	32 (9)	15 (12)	3 (23)	0.22
Uses recreational drugs ($n = 494$)	27 (8)	8 (6)	0 (0)	0.51
Corticosteroid use in last month ($n = 497$)	30 (9)	10 (8)	0 (0)	0.51
Hospitalization history ($n = 118$)				0.24
in past week	9 (11)	5 (16)	1 (14)	
1 week to 1 month	27 (34)	12 (39)	0 (0)	
1 month to 1 year	44 (55)	14 (45)	6 (86)	
Clinic visit history ($n = 208$)				0.37
in past week	15 (10)	6 (11)	1 (13)	
1 week to 1 month	39 (27)	11 (20)	4 (50)	
1 month to 1 year	91 (63)	38 (69)	3 (38)	
Antimicrobial use history				
current, any	267 (75)	91 (69)	10 (71)	0.41
in past year (any, $n = 497$)	167 (47)	65 (50)	7 (50)	0.86
doxycycline use within last year	54 (15)	27 (21)	1 (7)	0.23
trimethoprim/sulfamethoxazole use within last year	128 (36)	54 (42)	5 (36)	0.56
β-lactam use within last year	260 (73)	84 (65)	6 (43)	0.01
Hospital ward				0.001
surgical ward	69 (69)	23 (23)	8 (8)	
outpatient department	76 (76)	22 (22)	2 (2)	
maternity ward	80 (81)	17 (17)	2 (2)	
medical ward	64 (64)	34 (34)	2 (2)	
HIV clinic	65 (65)	35 (35)	0 (0)	

[a]Tests of association between cohort characteristics and the presence or absence of any SA colonization using χ^2 test for categorical variables or Fisher's exact test for cell sizes <5.

we found no association between chronic disease and SA colonization in our rural Ugandan setting. Here, recent β-lactam antibiotic use had a protective association against both MSSA and MRSA carriage and, though MRSA-positive samples were few, this finding merits further study.

Based on a small number of MRSA-positive samples, we also report a significant association between living or working with pigs and MRSA nasal carriage. Very few studies from sub-Saharan Africa report associations between animal contact and MRSA carriage, though several North American and European studies report

Table 2. Univariable and multivariable logistic regression analysis of factors associated with SA colonization

	Univariable		Multivariable	
Characteristic	OR (95% CI)	P^a	OR (95% CI)	P^a
Chronic diabetes mellitus	0	–	0	–
Male sex	1.71 (1.15–2.54)	0.008	1.68 (1.12–2.53)	0.01
β-Lactam use in last year	0.61 (0.40–0.91)	0.02	0.61 (0.38–0.97)	0.04
HIV infected	1.45 (0.97–2.17)	0.07	1.40 (0.91–2.14)	0.12
Open wound	0.69 (0.46–1.03)	0.07	0.94 (0.58–1.52)	0.79

[a]Tests of association between cohort characteristics and the presence or absence of SA colonization using univariable or multivariable logistic regression analysis.

a high prevalence of MRSA nasal carriage among pig farmers and their family members.[19,20]

Based on studies demonstrating that PCR-based detection methods are the gold standard for MRSA detection in low-prevalence settings,[16] we expect the Cepheid Xpert SA Nasal Complete assay performed well in our setting. However, our findings are limited by the cross-sectional study design, which does not allow for risk estimates or follow-up of colonized individuals. Use of a non-validated questionnaire and lack of specific testing for diabetes and other diagnoses could have led to reporting errors and misclassification bias. Additionally, due to resource limitations, we were unable to test for SA carriage from multiple body sites, perform MRSA genotyping, test for Panton–Valentine leucocidin or undertake more extensive antimicrobial susceptibility. Lastly, our inferences about factors associated with MRSA carriage are limited by the small number of MRSA-positive samples.

Knowing local SA and MRSA carriage prevalence can help guide clinical care and predict the likelihood of antibiotic-resistant infection. In south-western Uganda, we demonstrate low prevalence of the asymptomatic nasal MRSA carriage and that the MRSA carriage is associated with pig contact and surgical ward admission. Male sex was independently associated with SA carriage and recent β-lactam antibiotic use was associated with a mild protective effect against SA carriage. Future research on SA carriage in sub-Saharan Africa should focus on further elucidating risk factors for MRSA carriage and infection, particularly among surgical patients and people living or working with pigs.

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Transparency declarations

Cepheid Corporation (Sunnyvale, CA, USA) donated testing kits used in this study. Nothing else to declare.

Disclaimer

The content is solely the responsibility of the authors and does not necessarily represent the official views of Harvard Catalyst, Harvard University and its affiliated academic healthcare centres, or the National Institutes of Health.

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