Prevalence of methicillin-resistant *Staphylococcus aureus* nasal carriage among hospitalised patients with tuberculosis in rural KwaZulu-Natal

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Background. There is little information regarding the presence and characteristics of methicillin-resistant *Staphylococcus aureus* (MRSA), an important nosocomial pathogen, in rural African hospitals.

Objectives. To determine the prevalence of MRSA colonisation in patients admitted to a rural hospital with tuberculosis (TB) in an endemic HIV area and to describe transmission dynamics and resistance patterns among MRSA isolates.

Methods. A prospective prevalence survey in the adult TB wards of the Church of Scotland Hospital, a provincial government district hospital in Tugela Ferry, KwaZulu-Natal. Patients were eligible if over the age of 15 and admitted to the TB wards between 15 November and 15 December 2008. Nasal swabs were cultured within 24 hours of admission and repeated at hospital-day 14 or upon discharge. Susceptibility testing was performed with standard disk diffusion. Demographic and clinical information was extracted from medical charts.

Results. Of 52 patients with an admission nasal swab, 11 (21%) were positive for MRSA. An additional 4 (10%) of patients with negative admission swabs were positive for MRSA on repeat testing. MRSA carriage on admission was more common among patients with previous hospitalisation, and among HIV-infected patients was significantly associated with lower CD4 counts (p=0.03). All MRSA isolates were resistant to cotrimoxazole, and 74% were resistant to ≥5 classes of antibiotics; all retained susceptibility to vancomycin.

Conclusions. A high prevalence of multidrug-resistant MRSA nasal carriage was found. Studies are needed to validate nosocomial acquisition and to evaluate the impact of MRSA on morbidity and mortality among TB patients in similar settings.

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Methicillin-resistant *Staphylococcus aureus* (MRSA) is a serious global pathogen. The few reports of MRSA prevalence from Africa describe hospital epidemiology from large institutions in urban settings or aggregate data from referral laboratories.[1-4] Hospitalised patients with TB have high rates of HIV co-infection in sub-Saharan Africa that may increase risk of MRSA colonisation and infection. In a study from Cape Town, 53 (18%) of 291 patients with TB and HIV infection who had clinically deteriorated had another bacterial infection, including MRSA.[5] The presence and impact of MRSA among patients from rural hospitals in sub-Saharan Africa has not previously been studied.

KwaZulu-Natal Province has one of the highest rates of HIV co-infection among TB patients. At the rural hospital in Tugela Ferry, approximately 90% of patients admitted to the TB ward were found to be HIV-infected.[6] Routine hospital surveillance from Tugela Ferry identified patients with MRSA. Therefore, we studied the prevalence of MRSA colonisation in patients admitted to the TB wards and sought to describe resistance patterns among MRSA isolates, and the contribution of nosocomial acquisition.

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Methods

Patients and setting

Infection control staff performed a prospective prevalence survey of MRSA carriage among patients admitted to the adult TB wards at Church of Scotland Hospital in Tugela Ferry from 15 November to 15 December 2008. The hospital has 355 beds with occupancy of approximately 50 patients in both male and female TB wards. The hospital management and the local district's department of health initiated the survey. Patients provided consent prior to assessment.

A single swab was taken from the anterior nares of patients within 24 hours of admission to the TB wards and transported at room temperature to the referral microbiology laboratory, plated for culture on the same day and incubated at 37°C. Growth and identification were conducted on mannitol salt agar, with colony morphology on nutrient agar. The next day, suspicious colonies had a Gram stain performed. Identification of *S. aureus* was confirmed by a positive catalase and coagulase test. Susceptibilities were performed by standard disk diffusion method.[7] Repeat nasal swabs were obtained at hospital-day 14 or upon discharge if preceding the 14 days, and the presence or absence of MRSA was determined for each case.

Data from medical charts included age, sex, history of prior hospitalisation within the last 2 years, TB treatment history, HIV status, CD4 count (cells/mm^3) and current antibiotic exposures. Chi-square tests were used as appropriate and Mann-Whitney U-tests for non-parametric variables to compare clinical characteristics among patients with and without MRSA on admission.

Results

MRSA nasal carriage

During the study, 55 patients were admitted and 52 consented for survey. From the admission swabs, 13 (25%) patients had *S. aureus* isolated; 11 (85%, or 21% of total) of these had MRSA (Table I), while the remainder were methicillin-susceptible. Of patients with MRSA on admission, 9/11 (82%) had been previously hospitalised, compared with 17/41 (41%) patients without MRSA (p=0.08). Among known HIV-infected patients, those with lower CD4 counts were significantly more likely to have MRSA on admission (p=0.03). At follow-up on day 14 of hospitalisation, among 41 patients initially negative for MRSA, 4 (10%) were positive for MRSA.

Table I. Demographics and clinical characteristics on admission to TB ward compared by MRSA status; *N*=52

Characteristics	MRSA (+)	MRSA (-)*
Patient *N* (% total *N*)	11 (21)	41 (79)
Median age (IQR)	36 yrs (32 - 44)	35 yrs (28 - 44)
Sex		
Female (%)	6 (55)	18 (44)
Male (%)	5 (45)	23 (56)
Hospitalised last 2 yrs (%)	9 (82)†	17 (41)
On TB treatment (%)	11 (100)	41 (100)
HIV status		
Positive (%)	9 (82)	35 (85)
Negative	1 (9)	1 (3)
Unknown	1 (9)	5 (12)
Median CD4 count (IQR)	37 cells/mm^3 (20 - 60)‡	127 cells/mm^3 (47 - 190)
Receiving cotrimoxazole (% of HIV-infected)	7 (64)	24 (59)

*Four (10%) additional patients who were initially negative for MRSA had a positive follow-up culture.
†p=0.08.
‡Available in 41 (93%) HIV-infected patients, p=0.03. No other clinical characteristics were significantly different on admission.
IQR = interquartile range.

Including both admission and follow-up cultures, there were 15 patients with MRSA who produced a total of 19 isolates. Of the patients with MRSA, 9 (60%) had previously received cotrimoxazole as part of prophylaxis for opportunistic infections. All patients with MRSA were receiving first-line therapy for TB with rifampicin, isoniazid, pyrazinamide and ethambutol. Additionally, 2 patients were receiving ampicillin and gentamicin, and 6 were receiving a cephalosporin.

MRSA resistance patterns

All 19 MRSA isolates were resistant to cotrimoxazole, penicillin, ampicillin and gentamicin (Table II). Of 18 isolates tested for susceptibility to tetracycline, 15 (83%) were resistant; 14 (74%) of isolates were resistant to erythromycin and, although only 12 were tested against clindamycin, all were susceptible. Additional testing for the macrolide-lincosamide-streptogramin B (MLS_B) phenotype using the D-test among erythromycin-resistant isolates was not performed. All isolates were susceptible to vancomycin and 89% to fusidic acid.

Table II. Susceptibility patterns of MRSA isolates; *N*=19

Antibiotic	S	I	R	% R
Penicillin	0	0	19	100
Ampicillin	0	0	19	100
Oxacillin	0	0	19	100
Gentamicin	0	0	19	100
Cotrimoxazole	0	0	19	100
Tetracycline	2	1	15	83
Erythromycin	5	0	14	74
Clindamycin	12	0	0	0
Fusidic acid	17	2	0	0
Vancomycin	19	0	0	0

S = susceptible; I = intermediate; R = resistant. Antibiotic disk concentrations per recommendations of Clinical and Laboratory Standards Institute (formerly National Committee for Clinical Laboratory Standards).[7]

Discussion

This first report of MRSA nasal carriage in hospitalised TB patients from rural South Africa demonstrates high admission prevalence and possible additional new MRSA acquisition during hospitalisation. Among new admissions to the TB ward, 21% were carriers of MRSA. Strikingly, 90% of all *S. aureus* isolates from the nares of predominantly HIV-infected patients were MRSA, a rate much higher than existing data from the province. In an extensive study of all clinical isolates of *S. aureus* from KwaZulu-Natal, only 27% were MRSA.[8] Although mechanisms of resistance were unable to be further characterised, it is notable that HIV-infected patients with advanced immunosuppression were more likely to carry MRSA.

This study also suggests an ominous trend regarding susceptibility to other antimicrobial agents among MRSA isolates. Although only 60% of the patients with MRSA carriage had received cotrimoxazole prophylaxis, all recovered MRSA isolates were resistant to cotrimoxazole. All MRSA isolates were resistant to ≥3 antibiotic classes, 79% resistant to 4 classes, and 74% resistant to 5 classes. Although susceptibilities to rifampicin were not performed on these multidrug-resistant isolates, high levels of rifampicin resistance from MRSA clinical isolates in KwaZulu-Natal have been noted.[8]

Definitive molecular investigation was not available, and the additional MRSA positivity found in the follow-up swabs might have been the result of intermittent carriage or poor technique on the first collection. However, among those with MRSA nasal carriage, available susceptibility patterns and the high rate of previous hospitalisation suggest nosocomial acquisition.

This small study underscores the need for larger-scale studies of the epidemiology of MRSA in rural South Africa, the presence of which has important clinical consequences. Identification of MRSA and reduction in empiric use of courses of expensive antibiotics that may not be of benefit require improved and more accessible laboratory capability. Unfortunately, multidrug-resistant MRSA infections may only remain susceptible to vancomycin or newer glycopeptides. In South Africa's public sector, vancomycin is a restricted medication in rural hospitals and often available only upon demonstration of a drug-resistant organism.

We also highlight the need to implement sound infection control practices. Most rural hospitals in sub-Saharan Africa have limited resources for such implementation. Patients admitted to the Tugela

Ferry hospital or similar district hospitals are not routinely screened for MRSA carriage, and neither are patients cohorted based on current or prior MRSA infection. Hand-washing facilities and practices are sub-standard. The legitimate fear of airborne TB transmission in similar settings might have drawn attention from other virulent hospital-acquired infections whose transmission is largely preventable by hand hygiene and identification of infectious hosts and carriers.

Conclusions

A high prevalence of multidrug-resistant MRSA nasal carriage was found among TB patients with advanced HIV admitted to a rural hospital in South Africa. Nosocomial transmission was suggested by previous hospitalisation history, similarity of antibiotic resistance and possible further acquisition during hospitalisation. Prospective studies are needed to validate the high carriage rate and nosocomial acquisition as well as to evaluate the impact of MRSA on morbidity and mortality among TB patients in similar settings, and expand the evidence base for enhanced microbiological and infection control resources, policies and practices.

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