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MICROBIOLOGY

The epidemiology of *Staphylococcus aureus* skin and soft tissue infection in the southern Barkly region of Australia's Northern Territory in 2017

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Summary

The aim of this study was to describe the burden and organism antibiotic resistance patterns of skin and soft tissue infections (SSTI) due to *Staphylococcus aureus* presenting in a remote Australian Northern Territory community in the Barkly region.

We collated reported antibiograms of all skin and superficial soft tissue swab specimens obtained from the town's Indigenous medical clinic from 12 of the 13 months between November 2016 and December 2017. Clinician's notes for the consultation associated with each test request were examined to determine the nature of the clinical problem and to access other relevant data.

Amongst 309 tissue swab specimens, *S. aureus* was cultured in 215 (70%), of which 202 isolations were from Indigenous Australians. Of the 215 *S. aureus*, 98 [46%, 95% confidence interval (CI) 31–52] were methicillin resistant *S. aureus* (MRSA) and 117 (54%, 95% CI 48–61) sensitive (MSSA). Significant numbers were also resistant to other frequently used oral antibiotics, with resistance to erythromycin in 52 (24%), clindamycin in 51 (24%), trimethoprim in 22 (10%) and fusidic acid in eight (4%).

In the Barkly region of Australia's NT in 2017, community-acquired staphylococcal SSTI needing professional care is equally likely to be caused by MRSA as by MSSA.

Key words: Skin and soft tissue infections; *Staphylococcus aureus*; *S. aureus*; methicillin resistance; treatment protocols.

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INTRODUCTION

There is a heavy burden of skin and soft tissue infections (SSTI) caused by *Staphylococcus aureus* in remote Australian communities.

Recent studies have examined adults with SSTI admitted to the Alice Springs Hospital (the ASH)[1] and children with impetigo,[2] and there are broader laboratory based studies of overall resistance rates of *S. aureus*.[3,4] Gaps thus exist in our knowledge of the incidence and clinical features of staphylococcal infections across the age spectrum in remote communities, and we are not aware of any reports that have previously documented the epidemiology in the Barkly region specifically.

We describe here the burden of SSTI where *S. aureus* was recovered from lesions patients presented to the Anyinginyi Health Aboriginal Corporation (AHAC) Health Centre in the remote Australian community of Tennant Creek, Northern Territory (NT), over one year from November 2016. AHAC also provides an outreach service, which serves selected parts of the Barkly district from approximately Wauchope in the south to Corella Creek in the north. It attends all Indigenous Australians who present for care (with 2,957 currently enrolled) and also non-Indigenous Australians who have lived in the Barkly for at least two years (with 1,213 currently enrolled). There is a small NT government hospital also in Tennant Creek, with a continuously working emergency department staffed by general medical practitioners. The regional tertiary level hospital, the ASH, is 505 km south at Alice Springs.

METHODS

Both the AHAC Board and the Central Australian Human Research Ethics Committee approved this study (HREC reference CA-18-3143).

The population studied is enumerated in the 2016 Australian census.[5] It recorded 2,995 residents in Tennant Creek, 1,536 (51.3%) of whom identified as Indigenous. In spite of the remarkable mobility of the Indigenous population, which has been noted by the Productivity Commission,[6] in 2011 the respective numbers were 3,062 and 1,591 (51.9%),[7] indistinguishably similar.

Since 201 of the 213 patients studied here were residents of Tennant Creek itself, we thus chose to use as the denominator in the pertinent calculations the 2016 Census figures of people resident there; we have allocated ancestry to the small proportion of people with unstated ancestral status in the proportions seen in the majority. We focus in Tennant Creek.

We obtained data through a query of the AHAC clinic pathology report listing of all tissue swab specimens as provided by the clinic's pathology testing provider, Western's Diagnostic Pathology, for 12 of the 13 months from November 2016 to December 2017. The clinician's notes for the consultation that contained the pertinent test request were examined (by RXD) to verify the nature of the clinical problem, described variably as boils, sores and abscesses, (many being multiple), and infected burns and wounds. Screening specimens, e.g., nasal and perineal swabs, were excluded.

The age, gender and ancestral identification of each patient and his or her glucose metabolism and renal function status were noted. If *S. aureus* was recovered more than once from an individual, this was counted as a single episode if the samples demonstrated the same antibiogram. Otherwise, they were counted as separate episodes. For incidence calculations, only one episode per individual was included. Result patterns between swabs from patients dwelling within the same household were noted.

Antibiotic susceptibility testing of each *S. aureus* isolate was performed for penicillin, flucloxacillin, cephalexin, erythromycin, clindamycin,

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trimethoprim-sulfamethoxazole (i.e., SXT, cotrimoxazole), fusidic acid, rifampicin, ciprofloxacin and vancomycin, according to Calibrated Dichotomous Susceptibility test methods and criteria. Recent work by Harris *et al.* has shown that within the trimethoprim-sulfamethoxazole combination, resistance is usually only found to the trimethoprim component.[8] We have incorporated this finding here. We defined methicillin resistance or susceptibility, respectively, as concordant resistance or susceptibility to flucloxacillin and cephalexin, respectively MRSA and MSSA.

RESULTS

During the 12 months studied, 309 specimens satisfied inclusion criteria. Detailed results are shown in Table 1.

Eight patients were swabbed on more than one occasion. In three patients *S. aureus* cultured twice during the year shifted to methicillin resistance; only the resistant strain was counted. Two patients who were swabbed twice grew organisms with differing antibiograms; both were included.

Of the 215 (70%) swabs which grew *S. aureus*, 202 were from Indigenous Australians. Whilst the small, 6%, proportion of non-Indigenous patients' isolates seen here does not permit extensive comment on the nature of resistance in any microorganism they might harbour, it is pertinent to note that in the study period such patients constituted 29% of all patients enrolled at the AHAC clinic. Had they presented with SSTI lesions similar to those seen in the Indigenous 71% enrolled, it is likely that they too would have had their lesions swabbed. Moreover, only two (15%), of their 13 *S. aureus* were MRSA vs the 48% in the Indigenous patients (Fisher p for the difference <0.041). We should exercise care in drawing inferences therefrom, but the data suggest not only that MRSA is endemic in Tennant Creek, but that it may be confined largely within the Indigenous sub-community.

No statistically significant difference was seen between the genders (Fisher $p>0.17$) and thus males' and females' results are aggregated. MRSA were cultured also across the entire age spectrum of AHAC's patients (Table 1).

Of the 215 *S. aureus* cultured, 98 were MRSA, [46%, 95% confidence interval (CI) 31–52%], and 117 were MSSA, (54%, 95% CI 48–61%). Two of the MSSA organisms also remained sensitive to penicillin. Amongst all cultured *S. aureus*, concomitant resistance was found to erythromycin in 52 specimens (24%), clindamycin in 51 specimens (24%), fusidic acid in eight (4%) and cotrimoxazole in 22 (10%), although as noted in section 2, this is likely to be resistance only to cotrimoxazole's trimethoprim component. Seven MRSA isolates were resistant to other antibiotics, six with resistance to erythromycin and clindamycin, and to fusidic acid. The laboratory reported only one further multi-resistant isolate, from a 6-year-old child, resistant to clindamycin, cotrimoxazole, rifampicin and *(sic)* vancomycin.

Table 1 Study findings: organism details and host and organism characteristics

	n	% of total	Organism details				
			All *S. aureus*	MSSA		MRSA	
				n	%[a]	*n*	%[a]
Host characteristics							
Age group (years)							
0–9	318	19	48	24	21	24	24
10–19	269	16	26	14	12	12	12
20–29	321	19	40	22	19	18	18
30–39	226	14	20	13	11	7	7
40–49	231	14	29	14	12	15	15
50–59	160	10	36	19	16	17	17
60–64	54	3	7	6	5	1	1
≥65	88	5	9	5	4	4	4
All	1667		215	117		98	
Gender							
Male	115		115	68	59	47	41
Female	100		100	49	49	51	51
All	215		215	117		98	
Ancestry							
Indigenous	202		202	106	52	96	48
Non-Indigenous	13		13	11	85	2	15
All	215		215	117		98	
Concomitant disease							
People with T2DM			67	35		32	
People on renal dialysis			7	2		5	
Organism characteristics							
Also resistant to							
Erythromycin			52	33	28	19	19
Clindamycin			51	32	27	19	19
Trimethoprim[b]			22	0	0	22	22
Fusidic acid			8	0	0	8	8
Co-cultured organisms							
GAS			117	70	60	47	48
Other group streptoccoci			10	7	6	3	3

GAS, Group A Streptococcus; MRSA, methicillin resistant *S. aureus*; MSSA, methicillin sensitive *S. aureus*; T2DM, Type 2 diabetes mellitus.
[a] % of sub-group total.
[b] See text for explanation.

The high rates of clindamycin and erythromycin resistance seen in the MSSA isolates may reflect circulation of plasmid-mediated resistance mechanisms in the MSSA population whereas lower rates in MRSA isolates may indicate expansion of particular MRSA clones that do not harbour these plasmids. However, we are unable to further determine the underlying mechanisms without more detailed genotyping of isolates.

If the same rate of infection, disease, and organism isolation persists, then in the NT's southern Barkly region served by AHAC, the Indigenous population incidence of SSTI of such severity as to bring the sufferer to the clinic would be 181/1,000 people per year (95% CI 163–200/1,000/y). The prevalence of *S. aureus* isolations therein would be 129/1,000 people (95% CI 114–146/1,000), and of MRSA, 59/1,000 (48–71/1,000).

Concomitantly cultured bacteria included 117 group A streptococci (GAS) (54%, 47–60%), two group B, four group C and four group G streptococci; one *S. lugdunensis* was grown.

Type 2 diabetes mellitus (DM2) was common and present in 66 of the 143 adults ≥20 years of age and from whom also *S. aureus* was cultured, 46% (39–55%). Renal function data were available for 64 of the 66; function was variably well maintained. Of the 64, 32 had an eGFR >90 (all, mL/min/1.73 m^2), 18 had eGFRs between 60 and 90 with variable levels of urinary protein loss, and 14 had an eGFR <60 (seven of whom were treated with haemodialysis). The prevalence of DM2 increased with increasing age and finally stabilised, being diagnosed in 65% (55–75%) of people ≥40 years of age, and 67% (53–78%) at ≥50.

DISCUSSION

Findings

Like Tong *et al.*,[3] we have deployed data directly from community clinical service sources and also have the added advantage of having been able to scrutinise the pertinent clinicians' clinical notes. Further, serendipitously, the microbiological data in both studies derive from the same private pathology firm's laboratory. All this continues to meet the WHO challenge to derive such data from other than hospital-based resistance antibiograms.[9] Selection bias was also reduced because no sub-sampling amongst the presenting patients was involved. The entire town's entire Indigenous population was the study population for the 12 months surveyed.

In the southern half of Australia's NT, community-acquired staphylococcal infection producing SSTI needing professional care in 2017 is equally likely to be caused by an MRSA as by an MSSA. These findings are then reflected in the organisms cultured from people admitted to hospital for inpatient care of such disease, the MRSA prevalence in the Barkly community being 46% and 57% at ASH.[1]

The ubiquity of the MRSA in our communities is reinforced by its presence evenly across all age deciles, and in its being isolated from different members of the one, house-sharing family, each with an identical antibiogram. Its prevalence, and that of MSSA, align very similarly with the numbers of people alive within most decades, as shown in Table 1. This finding may not have been readily appreciated before now, possibly because most studies in communities have focussed more on children than across the entire age spectrum.

The challenging nature of the local Indigenous domestic environment that leads to just such a push for ongoing selection in antibiotic resistance has been previously described by Tong *et al.* He noted that: 'High rates of scabies, skin, respiratory and ear infections, and the severity of these infections result in frequent courses of β-lactam antibiotics. Combined with domestic crowding within households and poor levels of functioning health hardware…for skin hygiene, this represents a potent mix for the ongoing selection for antibiotic resistance.'[3] RXD's own observations over the last decade on site, in the clinic and in the homes both in Tennant Creek and in the more remote Barkly, and now also Deloitte's recent authoritative review and report,[10] confirm that the scenario remains unchanged in 2017, as has the need to address it. Deloitte also confirms that the problem is seen across the entire NT.

By comparison with Tong *et al.*'s prevalence data for *S. aureus* and MRSA isolations, respectively, in all of the NT in 2001 (6.4/1,000 and 0.3/1,000) and in 2011 (54.5/1,000 and 13.0/1,000 people),[3] the findings detailed above demonstrate a significant increase in *S. aureus* isolations and in MRSA.

The high rates of GAS co-infection, however, are consistent with studies of impetigo in remote Australian communities where such co-infection is the usually observed, established, pattern.[11,12] Although GAS susceptibility to trimethoprim-sulfamethoxazole was not reported for our patients by Western's laboratory, recent studies from the NT have found the prevalence of resistance to it among GAS isolates to be ≤1%.[13] The use of trimethoprim-sulfamethoxazole for SSTI, including those associated with GAS, also has been supported by several recent studies.[11,14]

One insurmountable weakness in this study, and indeed in Tong's prior work, is that neither we nor he can assess the extent to which we underestimate the burden of the morbidity of SSTI in the communities studied. Though we are careful to say '…SSTI needing professional care', we should add 'in the opinion of the affected person'. We do not know the degree of the under-estimation of the real morbidity or of its change over these different periods; it is unlikely it will be over-estimated.

As well, the 2016 Census data leave unknown the ancestral identification of 247 people within Tenant Creek, 8.3% of the total. This may have resulted in either a slight under or over estimate of the extrapolated population incidence of infection and, within it, the prevalence of *S. aureus* isolations. The MRSA prevalence rates in the Indigenous population remain concerningly high.

The generalisability of our data might also be questioned. However, other studies from Central and Northern Australia provide a similar picture of high and rising rates of MRSA.[1,15] There is likely to be geographical variation in MRSA rates and local data such as that presented here are critically important as a guide to local prescribing practice (Fig. 1).

Going forward

Given that it is unequivocally impracticable to consider clearing MRSA from the local environment of the Barkly—it is there to stay until at least the Indigenous housing component of that environment changes—how are we to treat these

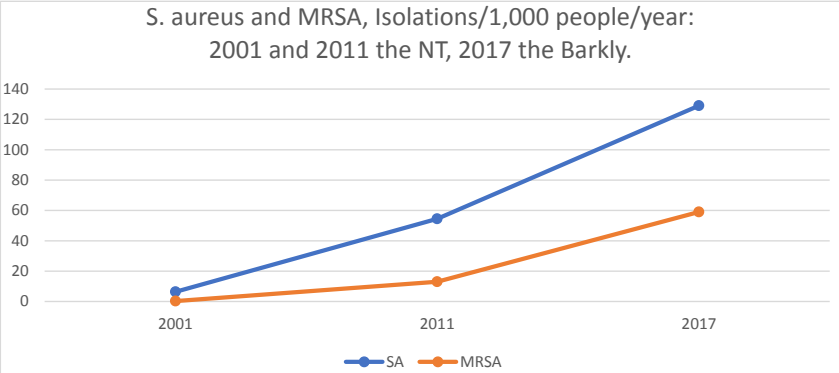

Fig. 1 Data for 2001 and 2011 are derived from the NT wide study of *Staphylococcus aureus* results from 1993–2012 cited from Tong *et al.* with permission.[3] The 2017 data are from this current study in the Barkly. The data all refer to total isolations of *S. aureus* and MRSA and hence will be related to both the incidence of skin and soft tissue infections, but also to testing practices at each time point.

SSTI in general practice, in the Barkly and in Australia at large?

It is apparent that there is considerable heterogeneity in rates of MRSA incidence in Australia. The incidence rate of about 50% we have found among the community derived *S. aureus* clinical isolates in the Barkly region is consistent as noted with the rate from the Alice Springs Hospital (57%).[1] Also, although there is a paucity of similar community based data from elsewhere in Australia, if hospital data reflect community data, then it is likely that the incidence rates of MRSA as a proportion of *S. aureus* infections are much lower in other regions; e.g., rates of MRSA in *S. aureus* bacteraemia are 47% in the NT, but only 16% in Victoria and 11% in Tasmania.[15] Therefore, antibiotic recommendations now need to be tailored according to local antibiograms.

Where the prevalence of MRSA approaches 50%, empiric β-lactam based therapy may no longer be the best option. In addition to emphasising the importance of incision and drainage of abscesses, and obtaining susceptibility data, recent evidence suggests that antibiotic therapy with either cotrimoxazole or clindamycin increases the rate of cure of lesions[16,17] and local advice concurs.[18] In the setting of the NT, we found the rate of resistance to clindamycin was 24%, and (not unexpectedly) clindamycin treatment failures have been found to be more common when clindamycin resistance is present.[16] A recent meta-analysis has also favoured the use of cotrimoxazole over clindamycin due to the increased risk of side effects with clindamycin.[19] Further supportive of a recommendation for cotrimoxazole to be first line therapy is the local evidence that cotrimoxazole is also effective against Group A Streptococcus, both in the laboratory[13] and in a clinical trial.[11] Concerns about potential for development of resistance to cotrimoxazole in *S. aureus* have been raised[20] and, as noted above in Section 2, more recent investigations have found inaccuracies with automated testing for cotrimoxazole resistance, such that further confirmatory phenotypic testing should be performed on apparently resistant isolates. It is likely that in most cases these isolates are trimethoprim resistant but susceptible to cotrimoxazole, i.e., the co-formulated trimethoprim and sulfamethoxazole.[8] There is presently no evidence that cotrimoxazole resistance is a clinical concern; however, systematic monitoring is critically essential, especially if trimethoprim resistance does induce a lower threshold for the development of resistance to cotrimoxazole *per se*.

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