ORIGINAL RESEARCH ARTICLE

The prevalence of community-associated methicillin-resistant *Staphylococcus aureus* among outpatient children in a tertiary hospital: A prospective observational study in Riyadh, Saudi Arabia

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Abstract　*Background and objectives:* The emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) infections among previously healthy persons in community settings, without exposure to health care facilities, has been noted recently. Colonization rates of community-associated MRSA (CA-MRSA) have been reported to range from 0 to 9.2 percent. The nose and open skin areas are considered the most important sites for colonization. The aim of our study was to assess the prevalence and to describe the antibiotic susceptibility pattern of CA-MRSA among outpatient children.
Patients and methods: We prospectively screened every third consecutive child presenting to our pediatric emergency department of King Saud Medical City, a 275 bed tertiary care teaching hospital in Riyadh, Saudi Arabia, from March through July 2015.
Results: We analyzed a total of 830 screening results (n = 478 males, 57.6%). Most of the screened patients were from Riyadh (n = 824, 99.3%). A total of 164 (19.8%) were found to

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be colonized with *S. aureus*, and of these 38 (4.6%) with MRSA. Thus, the MRSA rate amongst all *S. aureus* carriers was 23.2%. All MRSA were susceptible to vancomycin, (94.7%) were susceptible to linezolid, (65.8%) to clindamycin, and (89.5%) to trimethoprim/sulfamethoxazole.
Conclusion: The rate of MRSA carriage among children in Riyadh province was within the range reported internationally. As the MRSA rate among *S. aureus* infected children was 23.2%, empirical MRSA coverage should be considered in children with suspected *S. aureus* infections.

1. Introduction

The emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) infections among previously healthy persons in community settings, without exposure to health care facilities, has been noted recently [1,2]. Community-associated (CA)-MRSA strains and healthcare-associated (HA)-MRSA strains differ in terms of epidemiology, microbiology, and clinical manifestations [3]. The rapid spread of CA-MRSA has been characterized by outbreaks of cutaneous infections in healthy individuals, but can also cause soft tissue and bone infections, sepsis and endocarditis, as well as necrotizing, frequently lethal pneumonia, especially after influenza infection.

Colonization rates of CA-MRSA have been reported to range from 0 to 9.2 percent [4]. The nose and open skin areas (e.g., wounds and device exit sites) are considered the most important sites for colonization [5,6]. Nasal carriage of MRSA is an important risk factor for subsequent MRSA infection and transmission of this pathogen [7].

Several studies have shown that the prevalence of CA-MRSA varies geographically. Global outbreaks have been reported from the United States (US) and New Zealand [8]. In a population-based surveillance study of three US communities in 2001–2002, 8%–20% of all MRSA isolates were CA-MRSA by definition, with the highest incidence among children <2 years old [9]. King et al also demonstrated that approximately two-thirds of all community-associated *S. aureus* skin infections in Atlanta were due to MRSA clones 300 [10].

The highest rates of CA-MRSA carriage (>50%) are reported in North and South America, Asia, and Malta. Intermediate rates (25–50%) are reported in China, Australia, Africa, and some European countries, such as Portugal (49%), Greece (40%), Italy (37%) and Romania (34%). Other European countries, including the Netherlands and Scandinavian Countries, have generally low prevalence rates. However, epidemiological data from separate studies are often not comparable, owing to differences in study design and populations sampled [11].

Although several studies have reported the prevalence of MRSA nasal carriage in patients in health care settings [12,13], this subject has been rarely investigated in healthy individuals in the broader community [14]. In Saudi Arabia, CA-MRSA was assessed by Fawzia et al in outpatient children at a university hospital from 2005 to 2008, where they found that 29.8% of clinical *S. aureus* isolates were CA-MRSA [15]. Of these cases, 64.7% were not associated with known risk factors. However, they evaluated clinical isolates rather than conducting active screening for MRSA. Another study on the prevalence of MRSA in the Western region of Saudi Arabia found that the prevalence of MRSA was 39.5% [16]. Infection was commonly associated with wound, skin, and soft tissue infections.

Currently, no data in Saudi Arabia on MRSA carriage in children is available. We aimed to assess the prevalence and to describe the antibiotic susceptibility pattern of MRSA among outpatient children in King Saud Medical City, a 1400 bed tertiary care hospital with a 275-bed children's hospital in Riyadh, Saudi Arabia.

2. Patients and methods

The study was approved by Research Advisory Council at this center. Informed consent was obtained from all legal guardians of participants.

2.1. Study design

We prospectively screened the anterior nares of children presenting to our pediatric emergency department of King Saud Medical City, a 275 bed tertiary care teaching hospital in Riyadh, Saudi Arabia, from March through July 2015.

Children under the age of 14 years who presented to the emergency department were eligible for the study. Patients who were hospitalized during the 12 months prior to their emergency visit, and those who were known MRSA colonizers, were excluded from the study. Thus, all newly detected MRSA colonizers in our study were defined as CA-MRSA.

Specimens were taken from each third consecutive patient meeting the inclusion criteria, and each patient was enrolled only once during the study period.

The attending emergency physician collected data on patient demographics (age, gender and history of recent hospitalization, antibiotic use and MRSA carriage).

2.2. Laboratory methods

A swab from each opening of the anterior nares were collected using pre-moistened sterile cotton swabs with normal saline solution, and were transported in Amie's transport medium.

Nasal swabs were processed within 2 h of collection and primary plating was done on mannitol salt agar (MSA)

without oxacillin to screen for *S. aureus*. After inoculation, plates were incubated at 35 °C in oxygen and read after 24 and 48 h. Each distinctive morphotype of mannitol fermenting colonies (yellow colonies) was selected from the MSA plate and sub-cultured on a 5% sheep blood agar plate. The colony was confirmed as *S. aureus* by catalase, slide coagulase (Staphaurex, Remel) and DNase tests. BD Phoenix™ Automated Microbiology System (Becton Dickinson, Franklin Lakes, New Jersey) was used for identification and antibiotics susceptibility testing for *S. aureus* species, which included testing for inducible clindamycin resistance. Tested antibiotics included: penicillin, oxacillin, erythromycin, clindamycin, sulfamethaxazole, vancomycin, linezolid, rifampin, ciprofloxacin and daptomycin. Any *S. aureus* that was resistant to oxacillin and/or cefoxitin was defined as MRSA.

2.3. Statistical analysis

The carriages rate was reported as the percentage of positive cases with *S. aureus* and MRSA colonization, respectively, out of the total number of patients sampled. Antibiotic susceptibility for patients colonized with MRSA was reported as the percentage of susceptible isolates out of total positive cases. We compared sex and age as risk factors for carriage using Chi-square statistics and Mann−Whitney U-test for non-normally distributed continuous data, respectively. A $P < .05$ was considered statistically significant. Statistical analyses were conducted using the SPSS version 18 (Chicago, IL).

3. Results

830 consented children were enrolled, (57.6%) were male. Most of the screened patients were from Riyadh (n = 824, 99.3%). A minority were from Asir (N = 4, 0.5%) and Alqasim (n = 2, 0.2%). A total of 164 (19.8%) were found to be colonized with *S. aureus*, and of those 38 (4.6%) with MRSA (Table 1). Thus, the MRSA rate amongst all *S. aureus* carriers was 23.2%.

The carriage rates were similar among males and females with an odds ratio (OR) of 1.31 (95% confidence interval (CI) 0.92−1.86; $P = .131$) for *S. aureus* carriage and 1.14 (0.58−2.21; $P = .708$) for MRSA, respectively.

The age of the patients ranged from 1 month to 13 years. The median age was 34 months (interquartile range (IQR) 12−68.25 months). The median age of *S. aureus* carriers was significantly higher (41.5 months, IQR 14.25−84.0) than in non-carriers (31 months, IQR 12.0−63.25) using the Mann−Whitney U-test ($P = .045$). The distribution suggests a higher rate in the very young that drops to a lower level

and then increases in older children (Fig. 1). Although the median age in MRSA carriers was higher than in non-carriers (60.0 versus 33.5 months), this difference was not statistically significant ($P = .246$).

Of the 38 cases colonized with MRSA, all isolates (100%) were vancomycin susceptible. Susceptibility rates for other antibiotics were 94.7% for linezolid, 65.8% for clindamycin and 89.5% for trimethoprim/sulfamethoxazole, 55.3% for Erythromycin, 84.2% for Ciprofloxacin, 97.3% for Rifampin and 94.7% for Daptomycin (Table 2). Seven (18.4%) isolates were clindamycin inducible resistant.

4. Discussion

Since CA-MRSA was first reported in 1993, it continues to emerge, and nowadays, in many areas, it is more common than HA-MRSA strains [17]. We are not aware of any data on the prevalence of MRSA colonization among children in Saudi Arabia published to date. We found that 19.8% of children without previous hospital admission or known MRSA carriage who presented to our tertiary care emergency department were *S. aureus* carriers, and that 4.6% were colonized with MRSA, which is within the international reported range [4]. Given that we excluded children with a previous hospital admission and previously known MRSA carriers, this rate reflects the CA-MRSA rate in children presenting to our institution.

The MRSA rate among all *S. aureus* carriers was found to be 23.2%, consistent with the reported rate from infected children elsewhere [15]. Furthermore, we found no difference in *S. aureus* or MRSA prevalence rates between males and females. However, *S. aureus* carriers were older than non-carriers.

Given the higher percentage of MRSA among *S. aureus* carriers, MRSA coverage should be considered for all suspected moderate to severe Staphylococcal infections. All MRSA isolates were susceptible to vancomycin, and most of the isolates were susceptible to rifampin, linezolid, trimethoprim/sulfamethoxazole, daptomycin and ciprofloxacin. However, we found relatively low susceptibility rates to clindamycin and erythromycin (65.8% and 55.3%

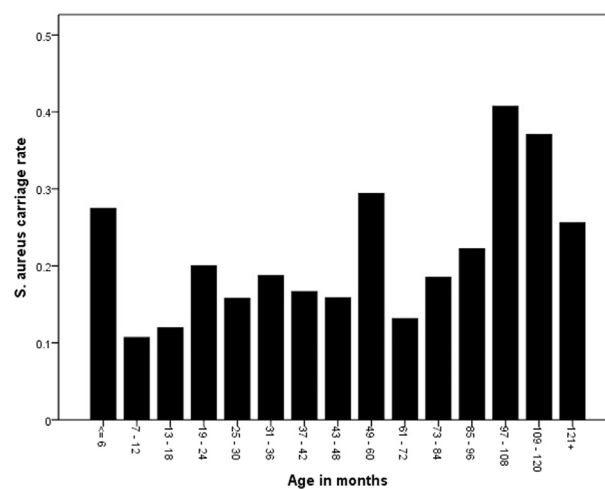| Table 1	*S. aureus* and MRSA carriage by sex.		
	Overall	Males	Females
	n (%)	n (%)	n (%)
Total	830 (100)	478 (100)	352 (100)
S. aureus carriage	164 (19.8)	103 (21.5)	61 (17.3)
MRSA carriage	38 (4.6)	23 (4.8)	15 (4.3)

Figure 1 *S. aureus* carriage by age group.

Table 2 Antibiotic susceptibility for MRSA.

Antibiotic	No. of sensitive isolates	Percentage
Vancomycin	38	100%
Linezolid	36	94.7%
Clindamycin	25	65.8%
Trimethoprim—sulfamethoxazole	34	89.5%
Erythromycin	21	55.3%
Ciprofloxacin	32	84.2%
Rifampin	37	97.4%
Daptomycin	36	94.7%

respectively) that would no longer justify the use of these antibiotics for empiric MRSA coverage. Vancomycin is the recommended empirical choice. However failure rate of vancomycin in CA-MRSA endocarditis is high even in combination therapy with gentamicin, and/or rifampin, particularly if vancomycin MIC is 2 μg/ml or more [18—20]. Daptomycin or linezolid as well as trimpethoprim/sulfamethoxazole could be used as an alternative treatment [21].

Other empirical choices include Lonezolid for CA-MRSA pneumonia and other moderate to severe infections apart from endocarditis or endovasculitis, and Trimethoprim—sulfamethoxazole for milder infections. These recommendations should be revised periodically based on annual antibiogram data.

To the best of our knowledge, this is the first study assessing the MRSA carriage rate in children in a Saudi Arabia setting. We collected data prospectively in a significant number of patients. However, this study also has a number of limitations. Firstly, it was a single center study and the rates may be different in other regions of Saudi Arabia. Furthermore, we conducted the study in a tertiary care emergency department setting, and the rates may be different in other settings, e.g. in patients seen by family physician.

Larger epidemiological studies would be needed to get a broader understanding of the prevalence and risk factors for MRSA, and in particular CA-MRSA carriage in the different provinces of Saudi Arabia.

5. Conclusion

The rate of CA-MRSA carriage among children in Riyadh province was within the range reported internationally. As the MRSA rate among children colonized with *S. aureus* was 23.2%, empiric MRSA coverage should be considered in patients with suspected moderate to severe *S. aureus* infections.

Conflict of interest

None.

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