Increasing Threat of Community-Acquired Methicillin-Resistant *Staphylococcus aureus*

Huda A. Bukharie, ABIM

Abstract: *Introduction:* Methicillin-resistant *Staphylococcus aureus* (MRSA) has emerged as a serious problem in the community. The objective of this prospective study was to report the frequency of community-acquired MRSA (CA-MRSA) isolates at King Fahd Hospital of the University in the Eastern Province of Saudi Arabia, to describe the spectrum of disease observed in patients infected with CA-MRSA and to study the antibiotic susceptibility profile. *Methods:* Isolates of CA-MRSA from King Fahd Hospital of the University were reviewed prospectively during an 8-year period, from January 2001 to December 2008. *Results:* The prevalence of CA-MRSA infections increased from 9.9 per 10,000 admissions in 2001 to 67 per 10,000 admissions in 2008 ($P < 0.001$). The number of CA-MRSA increased from 67 isolates in the first part of the study (2001–2004) to 176 cases in the second period of the study (2005–2008), and the percentage of CA-MRSA/of the total MRSA isolates rose from 20% in the first period to 59% in the second period of the study ($P < 0.001$). Soft tissue infections accounted for 198 (81%) of the 243 cases of CA-MRSA infections and invasive infections in 14 (7%) patients. The antibiotic susceptibility pattern has also changed with increasing levels of resistance to erythromycin, tetracycline, clindamycin, ciprofloxacin and gentamicin. *Conclusion:* Continued emergence of MRSA in the community is a public-health problem that demands increased vigilance in the diagnosis and management of suspected and confirmed staphylococcal infections.

Key Indexing Terms: *Staphylococcus aureus*; Saudi Arabia; Methicillin; Clindamycin. **[Am J Med Sci 2010;340(5):378–381.]**

The emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) infections in the community has become a serious public health problem in many parts of the world.[1–5] The growing prevalence and the substantial morbidity and mortality associated with these infections represent an evolving epidemic.[6] Hospital-acquired MRSA (HA-MRSA) commonly causes respiratory tract and bloodstream infections; community-acquired MRSA (CA-MRSA) has been isolated predominantly from skin and soft-tissue infections, such as abscesses, cellulitis, folliculitis and impetigo. However, potentially lethal and invasive infections, such as necrotizing pneumonia, fasciitis, pyomyositis, sepsis and toxic shock syndrome, in previously healthy patients have also occurred.[7–9]

In contrast to the multidrug resistance usually seen in HA-MRSA strains, antibiotic resistance in CA-MRSA strains is often limited to β-lactams. Most CA-MRSA isolates remain susceptible to tetracyclines, clindamycin, ciprofloxacin and trimethoprim-sulfamethoxazole (TMP-SMX). However, fluoroquinolone-resistant CA-MRSA strains have already emerged in some areas, and susceptibility to clindamycin can change over time.[10,11]

CA-MRSA infections were documented in our setting.[3] We have recently noticed an increased number of CA-MRSA infections in adults and children. This prospective study was undertaken to characterize the epidemiologic, clinical profile and antibiotic susceptibility patterns of CA-MRSA infections during an 8-year period from January 2001 through December 2008.

MATERIALS AND METHODS

Isolates of MRSA from King Fahd Hospital of the University, a 440-bed, primary-through-tertiary care hospital located in the Eastern Province of Saudi Arabia, were reviewed during an 8-year period from January 2001 to December 2008. Patients included in this study were considered to have CA-MRSA infection according to the definition of the Centers for Disease Control and prevention.[12] The Centers for Disease Control and prevention defines CA-MRSA as MRSA strains isolated in an outpatient setting or isolated from patients within 48 hours of hospital admission. These patients had no medical history of MRSA infection or colonization and no medical history in the past year of hospitalization, admission to a nursing home or dialysis. Furthermore, the patient lacked permanent indwelling devices such as catheters or other medical devices that pass through the skin.

Patient data were retrieved using the electronic hospital information system (containing patient demographics, results of imaging and other studies performed), and the medical records were reviewed. Patient data and isolate information (eg, demographics, underlying diseases, previous hospitalizations, primary diagnosis, hospital days and isolate antimicrobial susceptibility) were collected on a standardized form by the infection control team. A disease-associated isolate was defined to be responsible for the clinical syndrome of the patient, as determined by the site from which it was isolated, the physical examination and other relevant clinical data. Isolates not associated with disease were considered to be colonizing.

Invasive infections were those in the bloodstream, lymph nodes, mastoids, central nervous system, bone or joint, muscle, lungs or pleural fluid; superficial infections were of the skin, wounds and soft tissue other than of muscle and/or fascia.

The clinical microbiology laboratory performed antimicrobial susceptibility testing on *S aureus* isolates using the Vitek system (bioMerieux Vitek, Hazelwood, MO). An isolate was further evaluated with disk diffusion testing (Kirby-Bauer) if Vitek testing revealed it was resistant to oxacillin. MRSA isolates were tested for susceptibility to clindamycin, erythromycin, gentamicin, ciprofloxacin, rifampicin, TMP-SMX, tetracycline and vancomycin. The disk diffusion method outlined by the Clinical Laboratory Standards Institute (formerly National Committee for Clinical Laboratory Standards) was used to determine inhibitory zone size of tested antimicrobials.[12] The laboratory did not routinely perform the D-zone test for induc-

From the Infectious Disease Unit, Department of Internal Medicine, King Fahd Hospital of the University, Al-Khobar, Saudi Arabia.

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Correspondence: Huda Bukharie, ABIM, Infectious Disease Unit, Department of Internal Medicine, King Fahd Hospital of the University, PO Box 5746, Dhahran 3131, Saudi Arabia (E-mail: hudawe000@yahoo.com).

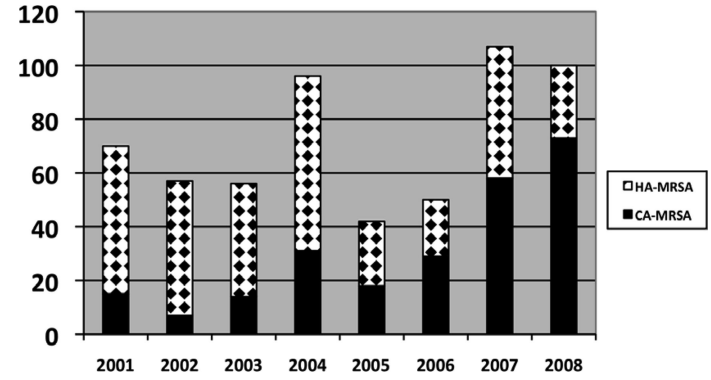

FIGURE 1. Prevalence of community MRSA isolates in King Fahd Hospital.

ible clindamycin resistance. Since 2008, oxacillin resistance has been confirmed by the detection of the *mecA* gene by multiplex polymerase chain reaction, which detects As442 fragment and mecA optimized for the Smart Cycler system (Cephied, Sunnyvale, CA).

MRSA rate was defined as the percentage of MRSA in all *S aureus* isolates. The incidence of CA-MRSA was defined as CA-MRSA per 10,000 admissions per year.

For comparison, the data were grouped into 2 periods: January 2001 to December 2004 and January 2005 to December 2008. Antibiotic susceptibility was analyzed by the χ^2 and the Fisher exact test. A P value of 0.05 or less was deemed statistically significant. The Z test for difference in proportion was used to compare the changes in proportion.

RESULTS

A total of 243 patients with CA *S aureus* infection fulfilled the criteria for inclusion in the study. The overall rate of MRSA among all *S aureus* infection isolates increased from 10% in 2001 to 16% in the year 2008 ($P = 0.0027$), and the incidence of CA-MRSA increased from 9.9 per 10,000 admissions in 2001 to 67 per 10,000 admissions in 2008 ($P < 0.001$). The number of CA-MRSA isolates increased from 67 (ie, 20% of all MRSA isolates) in the first period of the study (2001–2004) to 176 (ie, 59% of all MRSA isolates) in the second period of the study (2005–2008), an increase of 39% ($P < 0.001$). Figure 1 shows the number of CA-MRSA and HA-MRSA cases during the 8-year period.

The mean age of the patients was 34 years (ranging from 6 months to 82 years), and patients younger than 18 years constituted 31% (75 of 243) of cases. The majority of the patients were from Saudi (211, 87%), and among them, 136 patients (56%) were males. The spectrum of illness caused by CA-MRSA strains is shown in Table 1. Soft-tissue infections accounted for 198 (81%) of the 243 cases of CA-MRSA infections. However, invasive infections occurred in 14 patients (7%). Three patients (1%) had pneumonia, 6 patients (2.5%) had osteomyelitis and/or septic arthritis, 2 patients (1%) had adenitis and 3 patients had otitis (1%). Three patients had secondary bacteremia (1 with pneumonia, another with osteomyelitis and the third with an abscess). One patient with invasive MRSA died. This was a 68-year-old diabetic woman with CA pneumonia and bacteremia.

Two hundred eleven patients (87%) infected with MRSA did not have a predisposing factor or underlying condition. The most common risk factor identified was previous antibiotic therapy in 25 (10%) patients, diabetes mellitus in 16 (7%), eczema or asthma in 5 (2%) or 4 (2%), respectively, sickle cell anemia in 2 (1%) and had a household member with a history of CA-MRSA infection in 15 (6%).

A total of 134 (55%) of 243 patients were treated with an antimicrobial agent. Of 134 patients, including those with invasive disease who received antibiotics, 129 (96%) patients were initially treated with antimicrobial agents to which their MRSA isolates were not susceptible. Sixty-four patients (26%) required admission, and they eventually received appropriate antibiotic therapy. Of the 64 patients, 35 patients presented to the emergency room and were admitted immediately into the hospital where they received appropriate treatment. The other 29 patients were treated inappropriately, failed to improve and presented later with worsening of infection and required admission for treatment. One hundred fifty eight patients (65%) were treated with incision and drainage procedures, and 6 patients were treated with other surgical procedures (eg, joint drainage or debridement).

The rates of antibiotic resistance for CA-MRSA isolates are shown in Table 2. We compared the antibiotic-resistance profiles for the 2 study periods and for a previous time period between 1998 and 2000.[13]

Resistance to most of these agents increased substantially over the study period with dramatic increases observed with erythromycin and tetracycline. Resistance to antibiotics increased as follows: erythromycin from 5% in 1998 to 67% in 2008 ($P < 0.001$), tetracycline from 10% in 1998 to 42%

TABLE 1. Spectrum of illness caused by CA-MRSA

Infection	MRSA, n (%)
Pneumonia	3 (1)
Septic arthritis	2 (1)
Osteomyelitis	4 (2)
Bacteremia	3 (1)
Skin and soft tissue infection	
Cellulitis	25 (10)
Abscesses	165 (68)
Impetigo, folliculitis	8 (3)
Lymphadenitis	2 (1)
Suppurative otitis media	3 (1)
Tonsillitis	2 (1)
Conjunctivitis	3 (1)
Colonization	26 (11)

CA-MRSA, community-acquired methicillin-resistant *Staphylococcus aureus*.