COMMUNITY-ASSOCIATED INFECTIONS IN CHILDREN—UPDATE ON COMMUNITY-ASSOCIATED METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS FOR THE PRACTITIONER

Nationally, the incidence of infections in children due to resistant Staphylococcus aureus originating from the community (CA-MRSA) is increasing at alarming rates. The predominant clinical syndrome caused by CA-MRSA in children is skin and soft tissue infections (SSTIs), and many of these children suffer from recurrence of these SSTIs. Most studies published in the medical literature have evaluated infection and colonization due to resistant staphylococcal bacteria among people with previously identified risk factors, eg, indwelling catheters, chronic illnesses. Established risk factors for MRSA infection include recent hospitalization or surgery, stay at long-term care facility, history of prolonged antibiotic use, and history of injection drug use. However, little is known about the risk factors associated with CA-MRSA in children. This paper will summarize the current epidemiology surrounding CA-MRSA, the associated clinical syndromes and most common presentations, and the latest strategies to not only treat but to prevent the recurrence of the infections caused by this resistant bacterium, which originated from the community. (Ethn Dis. 2007;17[suppl 2]:S2-46–S2-49)

Key Words: Resistant Bacteria, MRSA, Community-Acquired Infection, Pediatrics

INTRODUCTION

Antibiotic-resistant bacteria are becoming an increasing problem in the United States and worldwide because they result in serious infections. These infections are occurring in a climate in which the availability of effective antimicrobial medications against resistant bacteria are becoming more limited. Historically, these resistant bacteria usually originate from hospital settings, where selection pressure drives resistance to a wide variety of antibiotic agents, presumably from repeated encounters with these drugs. However, one resistant bacterium is believed to have originated from the community and not from the hospital—community-associated methicillin-resistant Staphylococcus aureus (CA-MRSA). Although MRSA was identified in the 1960s, infections from MRSA previously occurred in individuals with established risk factors, which included history of indwelling catheters, chronic illnesses, recent hospitalization or surgery, stay at long-term care facility, prolonged antibiotic use, and injection drug use. Since the late 1980s and early 1990s, cases of MRSA infection among patients without such risk factors have been reported. These initial reports in the medical literature involved predominantly infections in children. Since then, CA-MRSA has been reported in a number of states all across the country. Patients who are infected with this bacterium are at increased risk for recurrent infections. To date, the risk factors for acquisition of this pathogen in children have not been fully defined.

MOLECULAR EPIDEMIOLOGY

Infections due to CA-MRSA in the United States has reflected primarily the emergence of two particular clones of MRSA, designated by the Centers for Disease Control and Prevention (CDC) as USA 300 and USA 400. These strains produce toxins such as Panton-Valentine leukocidin (PVL), which functions as a major virulence factor of these CA-MRSA clones. Specifically, the PVL cytotoxin is encoded by two genes, lukF-PV and lukS-PV. Panton-Valentine leukocidin (PVL) production is associated with severe forms of skin and soft tissue infections (SSTIs) and necrotizing pneumonia. Additionally, the presence of a staphylococcal chromosome cassette mec (SCCmeC) type IV allele has been associated with these strains. Within this small cassette lies the mecA gene, which is a hallmark of CA-MRSA strains. This mecA gene encodes a transpeptidase that has low affinity for β-lactam antimicrobial agents.

How the CA-MRSA virulence factors are related to colonization is not well understood. Boyle-Vavra et al have suggested that PVL is less often present in bacterial isolates associated with asymptomatic colonization. Pulsed-field gel electrophoresis is the standard method to detect genetic relatedness of CA-MRSA isolates. Specific sequence types (STs) have been associated with outbreaks by using multilocus sequence typing (MLST). The relationship between these STs and colonization has not been fully explored. The antibiogram susceptibility patterns and phenotype characteristic of these clones have consistently demonstrated resistance against β-lactam antibiotics and erythromycin. However, the distinction between CA-MRSA and hospital-acquired MRSA is no longer as clear, since more and more hospitalized patients harbor infections caused by strains of MRSA that had historically
COMMUNITY-ASSOCIATED INFECTIONS IN CHILDREN - Immergluck

originated from the community. For instance, in a three-year retrospective cohort study of children with CA-MRSA in Philadelphia, Zaoutis et al found many children with healthcare-associated infections caused by CA-MRSA strains. In their study, most of the children with and without risk factors for healthcare-associated infections harbored strains that carried the SCCmec IV cassette and produced PVL. The antibiograms were also similar in that most were susceptible to clindamycin, ciprofloxacin, and trimethoprim-sulfamethoxazole.

CLINICAL EPIDEMIOLOGY

Today, the prevalence of CA-MRSA infections continues to increase, and although some factors seem to predispose people to infection, a significant number of infections still occur in otherwise healthy people outside of an outbreak setting.

A recent CDC experts’ meeting on CA-MRSA indicated that the diseases caused by CA-MRSA have disproportionately affected young children, young adults, racial minorities, and lower socioeconomic groups. In their surveillance of 12 different facilities in Minnesota, Naimi et al found that CA-MRSA patients were more likely than healthcare-associated MRSA patients to be nonwhite (odds ratio 3.13, 95% confidence interval 2.16-4.32). In the population-based study by Fridkin et al, in which >12,000 patients with MRSA were identified in three communities (Baltimore, Atlanta, and parts of Minnesota), CA-MRSA incidence rates were much higher among Blacks in the Atlanta area across all age groups.

Although the specific risk factors for acquisition of CA-MRSA are not clearly delineated, crowding, sharing of personal hygiene items, or skin-to-skin contact appear to increase the risk for infection. A number of outbreaks of CA-MRSA infections have been reported among inmates in correctional facilities, participants of contact sports, military recruits, and attendees of day-care. Household transmission has clearly been demonstrated with CA-MRSA acquisition and subsequent infection. We cannot say why CA-MRSA was first noted in children and why, in population based studies, children continue to be the age group predominantly infected.

CLINICAL PRESENTATION

The Emerging Infections Program Network, a consortium of agencies (CDC, state health departments, participating universities), is tracking, through a population-based surveillance program, information on serious bacterial infections caused by CA-MRSA through the Active Bacterial Core Surveillance. This surveillance program does not track the most predominant clinical syndrome caused by CA-MRSA, which is SSTI.

Many superficial skin infections caused by CA-MRSA have been coined the “spider bite” masquerader, since the presentation is often confused with that of a spider bite. However, the range of skin infections that are due to CA-MRSA includes furuncles or “boils,” carbuncles, and abscesses. The severity of these skin infections can also vary from small, raised, red papules to draining and often necrotic lesions that extend into the soft tissue beneath the skin. Although SSTIs may account for the most common presentation, more severe and often life-threatening presentations include necrotizing pneumonia or empyema, joint or bone infections, septic shock, and necrotizing fasciitis. Adem et al described children hospitalized in Chicago with clinical symptoms and histologic findings due to CA-MRSA that caused a septic Waterhouse-Friderichsen syndrome. The patients who present with SSTIs appear to be at risk for subsequent recurrence of their SSTI.

CA-MRSA COLONIZATION

The relationship between colonization and infection with CA-MRSA is not well understood. In general, S. aureus colonizes 30%–50% of healthy adults. As for MRSA colonization, 7.3% of all adult patients admitted to a large public hospital in Atlanta were colonized with MRSA, and 2.2% of patients harbored a USA 300 clone, which is associated with origination from the community. This finding is in contrast to the 0.84% estimate, based on population based surveillance from the 2001–2002 National Health and Nutrition Examination Survey. Similar to nonresistant forms of S. aureus, studies in the medical literature show that once MRSA infections are treated, patients may still be colonized with MRSA, but we do not know what percentage of people persistently remain colonized. Although children appear to have higher persistent carriage rates, whether this carriage has any relationship as to why children are at higher risk for severe disease is unknown. Additionally, data suggest that persistent colonization may protect people from colonization by other strains. Some investigators have postulated that host factors are likely responsible for the determination of S. aureus carriage; whether or not this applies to CA-MRSA is unknown. Various protocols have addressed the efficacy of eradication of MRSA colonization among hospitalized patients. The success of eradication of MRSA has varied, ranging from 35%–95%. Loeb et al systematically reviewed the Cochrane database and other sources of the medical literature in 2003 for all randomized controlled trials of patients colonized with MRSA in an effort to determine the efficacy of different treatment strategies to eradicate MRSA.
They concluded that no evidence supported use of topical or systemic antimicrobial therapy for eradicating MRSA from colonized skin. Development of effective eradication of CA-MRSA colonization will depend on understanding the bacterial components that cause persistent colonization and how this may be tied to host factors, which support and maintain this existence.

**STRATEGIES FOR MANAGEMENT**

Most SSTIs are treated in the ambulatory setting. No standard guidelines exist on how to best treat CA-MRSA SSTIs empirically. The first objective is to determine the risk for CA-MRSA as the cause for the SSTI. Using local antibiotic susceptibility data as a general guide to treatment is a reasonable approach, so if there is a low prevalence of MRSA in the community, a β-lactam antibacterial agent can still be considered the first-line antibiotic. A methicillin resistance threshold of greater than 10%–15% among all S. aureus isolates in a community has been proposed by Kaplan as the empiric prevalence by which empiric treatment for SSTIs should include an agent effective against CA-MRSA. These oral agents primarily include clindamycin and trimethoprim-sulfamethoxazole. Tetracyclines have a limited role for the pediatric population, given they are not recommended for children under the age of eight years.

In certain select and specific situations, use of rifampin (only in combination with other effective agents) or linezolid can also be considered. When clindamycin is chosen, a “D-zone” test should be performed when possible. This test is necessary to identify those CA-MRSA isolates that have an inducible clindamycin resistance pattern. Because of increasing reports of clindamycin treatment failures, trimethoprim-sulfamethoxazole may be a better first-line agent to use in the ambulatory setting for SSTIs, even though it is currently not approved for the treatment of infections due to MRSA. For the treatment of abscesses, certain single lesions do not necessarily require antibiotics for treatment. For example, Lee et al has suggested abscesses that are smaller than 5 cm can be best treated by using incision and drainage, without antimicrobial therapy.

Selection of empiric antibiotic therapy for infections that require hospitalization is again based on MRSA antibiotic susceptibility data for that particular geographic area. In general, parenteral agents may include clindamycin, vancomycin, or linezolid. Some experts recommend adding nafcillin or oxacillin to cover for the possibility of severe infections due to methicillin sensitive staphylococci. To prevent recurrences in patients with repeated episodes of CA-MRSA SSTIs or prevention of hospital transmissions, pediatric infectious disease specialists have recommended various regimens, including using diluted bleach or chlorhexidine washes at regular intervals. However, no standard recommendations or published guidelines exist regarding the efficacy of these various anecdotal regimens.

**CONCLUSIONS**

CA-MRSA has received wide attention both in the medical and lay communities as the prevalence of cases continues to rise in many parts of the United States and worldwide. Understanding the pathogenesis of the virulence factors associated with these CA-MRSA strains and what host factors foster colonization and subsequent infection still need to be elucidated. With regards to the epidemiology of CA-MRSA in children, few studies have systematically and prospectively addressed whether or not race/ethnicity, younger age, specific geographic location, crowding, or socioeconomic status increase the risk for infection. Most of the published studies and reports are based on retrospective analysis over time as the number of cases of CA-MRSA continues to increase. Therefore, the epidemiology of this bacterium is still evolving as more and more infections continue to occur in different communities and populations—the distinction between which strains are community in origin and which are nosocomial becomes blurred. More population-based studies are needed to help define the true prevalence of this pathogen. Finally, since many of these patients infected with CA-MRSA present with recurring SSTIs, understanding the relationship between colonization and infection is paramount to prevent infection. Infection control policies and empiric antibiotic selections against CA-MRSA causing both noninvasive and invasive infections will need to be continually reassessed as this bacterium continues to evolve in both hospital and community settings.

**REFERENCES**


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