Methicillin Resistant Staphylococcus Aureus Skin Infection in Pediatric Patients

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Abstract

Objective: To investigate the prevalence, characteristics, and risk factors of methicillin resistant *Staphylococcus aureus* (MRSA) wound infection in a pediatric Emergency Department (ED).
Methods: The ED charts of a tertiary pediatric hospital were searched for all children who presented in 2005-2006 with a culture-proven skin infection. Background, clinical and laboratory data were compared between patients with MRSA and non-MRSA infections.
Results: MRSA was cultured in 171 of the 520 children (33%) identified. Mean age was 6±6 years in the MRSA group and 7±6 years in the non-MRSA group (p=0.06). Common sites of MRSA infection were the extremities (29%) and buttocks (26%); buttock abscesses were more prone to yield MRSA (26%) than non-MRSA isolates (12%) on wound culture (p=0.0001). Previously healthy patients acquired MRSA infections more often than patients with chronic conditions (22 v. 9%; p=0.0001). Compared with the non-MRSA group, patients with MRSA infection had higher rates of previous skin infections (24 v. 14%; p=0.006), earlier ED presentation (88 v. 77%; p=0.003), exposure to skin-infected household contacts (10% vs 2%, p=0.001), and history of insect bite(s) (20 v. 5%; p=0.0001). There were no between-group differences in prior physician visits (43 v. 46%; p=0.49), use of antibiotics within 14 days of the ED visit (32 v 32%; p=0.89), or daycare attendance (4 v. 2%; p=0.20).
Conclusions: MRSA infection is common in children and is associated with site of infection, previous history of cellulitis, previous history of insect bite to the area, health status and exposure to a household contact.

MeSH Words: methicillin resistant Staphylococcus aureus (MRSA), pediatric, antibiotics, soft tissue infection

Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) infection is a growing problem in both children and adults throughout the United States. Although it was initially associated with exposure in health-care settings, MRSA infection emerged in the late 1990s among previously healthy adults and children in the community [1-3]. The most common sites of community-associated MRSA infections are skin and soft-tissue; sometimes, cases can progress to invasive tissue infections, bacteremia, and death [4,5].

Recent studies have reported an increase in the incidence of MRSA infection along with descriptions of susceptibilities to different antibiotics [6,7]. Clinicians must be able to

recognize the spectrum of disease and the regional antimicrobial susceptibility patterns.
However, data on the prevalence of MRSA as a cause of skin infection in pediatric patients are still limited. The main aim of this study was to assess the prevalence of MRSA-induced skin infection in pediatric patients presenting to the Emergency Department (ED) of a large metropolitan-area pediatric tertiary medical center. The secondary aim was to identify risk factors that may help guide physicians in the ED when choosing antibiotics for children with skin cellulitis and abscesses.

Methods

The medical files of the ED of a tertiary pediatric medical center were searched for all children who presented between January 1, 2005 and June 30, 2006 with a skin infection that was diagnosed by wound culture. Patients in whom cultures were obtained from parts of the body other than the skin (i.e., joint aspirate, eye, ear, peritoneal or cerebrospinal fluid) were excluded as were patients who underwent repeated cultures and patients with missing or incomplete charts. The following data were collected from the files: age, sex, and ethnicity, source of culture and isolates, and blood cultures, if obtained. We also collected data from the patients' documented history, including: duration of symptoms, previous use of antibiotics (within 14 days to 3 months prior to the ED visit), history of insect bite, contact with others who had skin infections, attendance in a daycare center or other group settings, recent hospitalization (within 3 months of the ED visit), chronic medical diseases or chronic skin conditions, and previous episodes of cellulitis or abscesses. The ED course was also reviewed for data on presence of fever, treatment by incision and drainage (I & D), presence of a foreign body in the wound, and ED disposition (admitted or discharged home). For hospitalized patients, we tabulated length of stay and performance of I & D. Findings were compared between patients whose cultures grew MRSA isolates (MRSA group) and patients with infections due to other pathogens (non-MRSA group). In addition, the in vitro susceptibilities of all MRSA isolates from soft tissue cultures were analyzed.

The research protocol was approved by the local Institutional Review Board.

Statistical Analysis

Statistical testing was two sided using a type I error rate of 0.05. Analyses were performed with the SPSS (version 16; SPSS Inc., Chicago, IL). Chi-square test (χ^2) with Yates' continuity correction or Fisher's exact test was used to analyze associations between categorical variables. Highly skewed data were analyzed with the nonparametric Mann-Whitney rank-sum test and presented as median values and interquartile ranges (IQR: 25^{th}, 75^{th} percentiles). Continuous variables are presented as mean±standard deviation (SD) and were compared using the independent two-sample t-test. A multiple logistic regression model was used to assess the impact of a priori identified covariates on acquisition of MRSA infection. All candidate variables for logistic regression were considered; variables with a p value of 0.2 or less on univariate analyses were included in a forward stepwise selection. The final model presented in the paper includes history of previous skin infection, history of contact with others with skin infection, history of an insect bite, history of recent hospitalization, history of a chronic medical condition, and buttocks as a site of infection. Age, sex and race were included in the final multivariate analysis because of their potential influence on the outcome of interest. The results of the logistic regression model are presented as estimates of the odds ratio (OR) associated with specific covariates along with the 95% confidence interval (95% CI).

Results

During the 18-month study period, 672 patients presented to the ED with a skin infection. Those whose charts were missing or lacking vital data were excluded, leaving 520 patients for evaluation and analysis.

MRSA was isolated from wound cultures from 171 patients (33%). Mean age of the MRSA group was 6±6 years, and of the patients with infections due to other pathogens, 7±6 years (p=0.056). MRSA infection was more prevalent in females (37% v. 28%; p=0.023). By race, African-American patients were most likely to acquire MRSA infections (47%), followed by Caucasians (35%), Hispanics (31%), and Asian/Pacific Islanders (24%). Patients less than 2 years old, excluding newborns, were more

likely to have MRSA infection than other age groups (Figure 1).

Table 1 lists the results of the univariate analysis of potential risk factors. The most common sites of MRSA infection were the extremities and buttocks, and the least common, the genitals and axilla (Figure 2). Buttocks abscesses were associated with the greatest likelihood of yielding MRSA isolates in wound culture compared with other sites of infection (Figure 3). Compared with the non-MRSA group, the patients with MRSA infection had higher rates of previous skin infections (24% v. 14%; p=0.006), exposure to skin-infected household contacts (10% vs 2%, p=0.001), and a history of insect bite (20 v. 5%; p=0.0001). A history of a hospitalization within 3 months prior to presentation was associated with lower rates of MRSA infection, and previously healthy patients acquired MRSA more often than patients with chronic conditions.

There was a trend toward a shorter duration of swelling at the site of infection in the MRSA group (5±7 days v. 12±46 days; p= 0.06). More patients in the MRSA group presented to the ED within 7 days of illness (88% v. 77%; p=0.003), and more patients with non-MRSA infection presented later, within 7-14 days (12% v. 6%; p=0.026) or more (11% v. 5%; p=0.038). The MRSA group also had a higher rate of fever by history (41% v. 29%; p=0.007), although fewer patients in this group had fever in the ED compared to the non-MRSA group. There were no between-group differences in prior visits to a physician, use of antibiotics within 14 days of ED presentation, use of antibiotics within 3 months before the ED presentation, or daycare attendance (Table 1).

Fluctuance within the infected area was more often associated with MRSA than non-MRSA infection. Foreign bodies were present in the wound in only 1.2% of patients. I & D was performed in the ED in 32% of the whole sample, and in the department in 39% of the patients who were hospitalized. More patients in the MRSA group underwent I & D in the ED (58% v. 30%; p=0.000), but there was no between-group difference for I & D performed in the hospital department (37% v. 26%; p=0.27). There was no between-group difference in the rate of hospital admission (21% vs 30%, p=0.27). Median length of hospital stay was shorter for the patients with MRSA infection (3 days vs 4 days; range 2-5 days vs. 2-8 days), but the difference did not reach statistical significance (p=0.2).

Overall, 33% (n=171) of all soft tissue cultures obtained were positive for MRSA. Other predominant pathogens were methicillin-sensitive *Staphylococcus aureus* (MSSA), (n= 130, 25%), and β-hemolytic Streptococcus group A (n=33, 6%). All MRSA isolates were susceptible to vancomycin and 99% were susceptible to trimethoprim/sulfamethoxazole; 92% were susceptible to erythromycin, 85% to ciprofloxacin, and 6% to clindamycin. Blood cultures, which were obtained from 17% of the cohort, were negative for bacteremia in all cases. Of the patients who underwent blood culture, 38% were positive for MRSA isolates on wound culture, and 53% were positive for non-MRSA isolates. At discharge, 58% of the cohorts was prescribed clindamycin, 23% cefazolin, and 6% trimethoprim/sulfamethoxazole.

On multivariate logistic-regression analyses (Table 2), independent predictors of MRSA infection were previous history of episodes of skin infection, history of contact with others who had skin infections, history of an insect bite, and an unremarkable history without chronic medical conditions or recent hospitalizations.

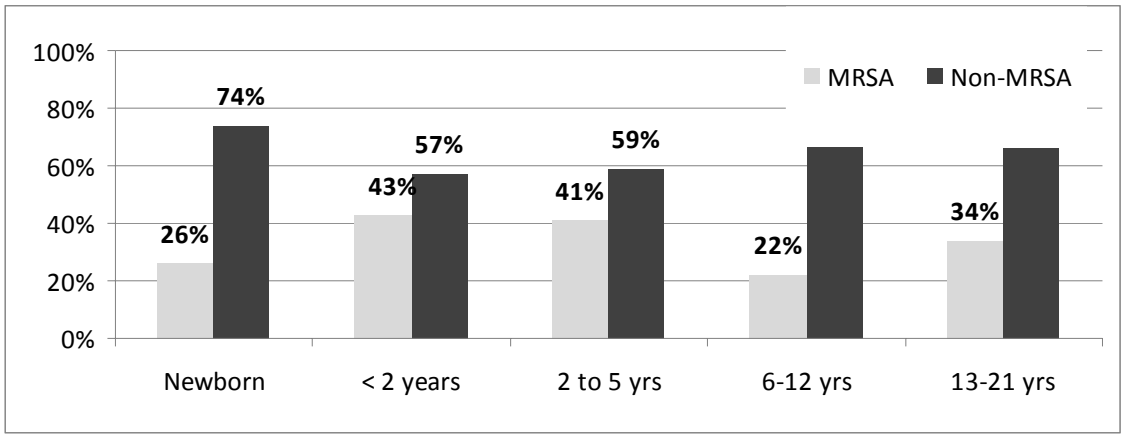

Figure 1. Age Distribution of MRSA and Non-MRSA Patients

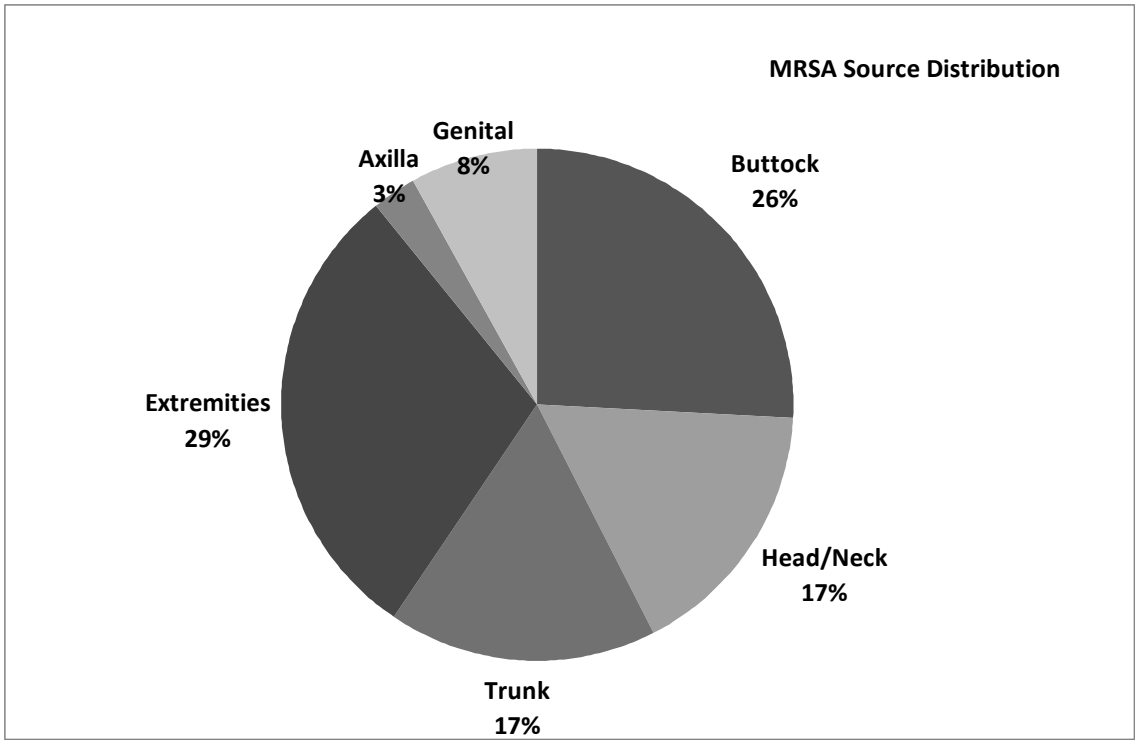

Figure 2. MRSA Source Distribution

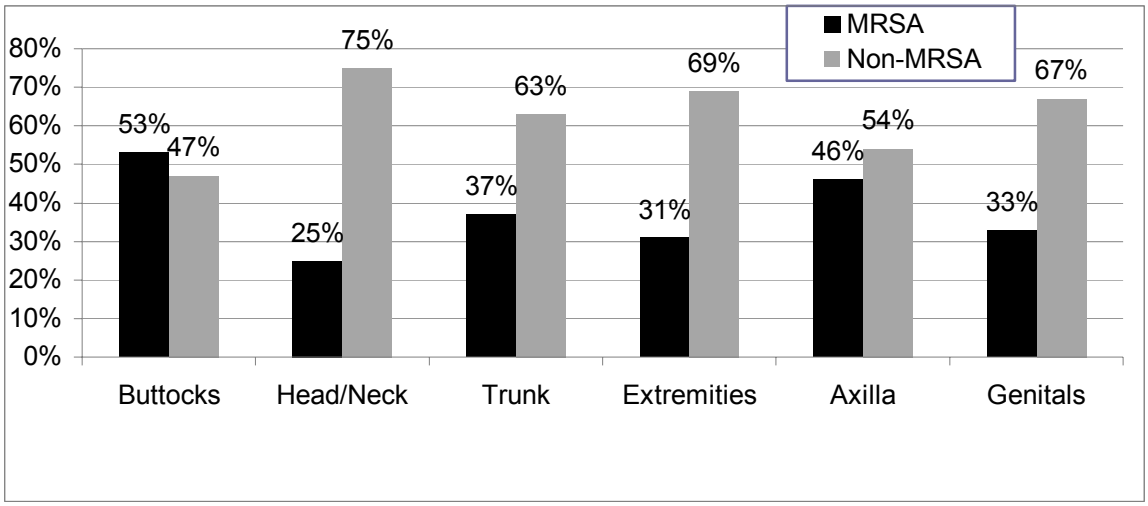

Figure 3. MRSA and non-MRSA Body Site Distribution

Table 1. Results of univariate analyses between patients with MRSA and non-MRSA skin infection*

Potential Risk Factor	MRSA Group (N=171)	Non-MRSA Group (N=349)	P Value
History of skin infections	39 (24%)	46 (14%)	**0.006**†
History of contact with others with skin infection	16 (10%)	5 (2%)	**0.0001**†
History of insect bites	32 (20%)	16 (5%)	**0.0001**†
History of hospitalization in previous 3 months	7 (4%)	52 (15%)	**0.0001**†
History of chronic medical conditions	15 (9%)	75 (22%)	**0.0001**†
History of chronic skin conditions	6 (4%)	23 (7%)	**0.14**
History of fever	68 (41%)	96 (29%)	**0.007**†
Buttock as site of infection	42 (26%)	38 (12%)	**0.0001**†
Extremities as site of infection	48 (29%)	106 (34%)	**0.59**
Fever in the ED‡	31 (19%)	43 (13%)	**0.07**
Physician visit prior to ED presentation	72 (43%)	158 (46%)	**0.49**
Antibiotics use in last 14 days	54 (32%)	109 (32%)	**0.89**
Antibiotics use in last 90 days	23 (14%)	39 (11%)	**0.46**
Day care attendance	6 (4%)	6 (2%)	**0.2**
Wound fluctuance	**72 (52%)**	**84 (31%)**	**0.0001**†

*Values are expressed as n(%); percentages are rounded to the nearest tenth. Missing values are excluded from the denominator of the percentages.
†$p<0.05$ was considered significant using chi-square test with Yates' continuity correction or Mann- Whitney rank sum test for comparisons.
‡Documented fever in the ED.

Table 2. Results of multivariate logistic regression analyses to identify risk factors of MRSA skin infection

Risk Factors	Odds Ratio*	95% CI†	P Value‡
History of previous skin infection	1.95	1.10 – 3.46	**0.022**
History of contact with others having skin infection	3.17	1.22 – 8.23	**0.017**
History of insect bite	3.16	1.80 – 5.56	**0.001**
No history of chronic medical conditions	0.45	0.22 – 0.88	**0.02**
No history of hospitalization in last 3 months	0.23	0.10 - 0.51	**0.001**
Buttock as site of infection	**2.10**	**1.20 – 3.60**	**0.008**

*Odds ratios were estimated from binary logistic regression model wherein outcome of interest (dependent variable) was MRSA in the wound culture.
† 95% confidence interval for the odds.
‡ A p value <0.05 was considered significant.

Discussion

The clinical determinants and associated risk factors for MRSA infection are unknown. The aim of the present study was to document the clinical characteristics and risk factors of MRSA infection in a pediatric population presenting to an ED of a large metropolitan area.

Moran et. al. [8] reported a 59% prevalence of MRSA infection in an adult population presenting with soft tissue abscesses in 11 EDs throughout the United States, with a range of 15% to 74%. In the Los Angeles area, where our study was conducted as well, estimates suggested that infection rates had risen from 29% in 2001 to 64% in 2004 [8]. In a retrospective chart review of cases of abscess requiring I & D at an urban tertiary care facility from 2003 to 2006, Pickett et al.[9] noted an increase in the incidence of MRSA infections, from 36% to 67%, over the duration of the study. In the present pediatric study, MRSA was isolated in 33% of cultures obtained from all children who presented with skin infection over a 1.5-year period, which was higher than the rate for MSSA cultured from soft tissue infection sites (25%).

Some previous reports noted a higher incidence of MRSA among children less than 2 years old of African-American descent [10-12]. In agreement, our study demonstrated that patients less than 2 years old, excluding newborns, acquired MRSA infections more often than other age groups, and the majority of patients with MRSA infection were of African-American descent.

We found that previously healthy children, with no medical problems and no history of hospitalization, were more susceptible to MRSA infection than children with chronic disease. This is congruent with the increased prevalence of MRSA infection within the Los Angeles community. The earlier ED presentation of the patients with MRSA, their higher rate of fever, and the trend in this group toward a shorter duration of swelling at the infection site, taken together, suggest that MRSA is an aggressive infection. This was further supported by findings of an increased rate of fluctuance, higher rate of I & D in the ED, and a trend toward a shorter hospital stay in the MRSA group. The factors identified on multivariate analyses to be predictive of MRSA skin infection were history of previous skin infection, history of contact with a household member who had had a previous skin infection and history of an insect bite at the area. We assume these are the most clinically relevant factors that physicians should address when obtaining a history from patients with skin infection or their caregivers in the ED. The buttocks as the site of infection also proved to be a major risk factor. Our findings confirm the factors identified by Moran et al. [8] in an adult population, and by others in pediatric populations according to 2002-2003 data [9,12-14].

Our study yielded no statistically significant difference between the groups in daycare attendance. Others, however, documented outbreaks of MRSA infection in childcare center attendees [15,16]. These outbreaks were likely to be sporadic and their occurrence was not

generalizable in terms of overall incidence of MRSA in the community. Also, some studies suggested that frequent exposure to antimicrobial agents may facilitate acquisition of MRSA [17,18]. However, we found no difference between the MRSA and non-MRSA groups in visits to a physician or use of antibiotics prior to the ED presentation.

Besides associated risk factors and infection site, the initial empiric therapy administered for suspected MRSA infection is influenced by the regional antimicrobial susceptibility patterns of the organism isolated as well as the severity of the infection. Various antibiotics, including clindamycin and trimethoprim–sulfamethoxazole, have been proposed for outpatient therapy for skin infections possibly caused by MRSA [19-21]. However, induced resistance to antimicrobial agents, especially clindamycin, has been reported [22,23], in addition to reduced susceptibility of MRSA to vancomycin [24,25]. In our study, all MRSA isolates retrieved from skin cultures were susceptible to vancomycin, and 99% were susceptible to trimethoprim/sulfamethoxazole; 92% were resistant to erythromycin, 85% to ciprofloxacin, and 6% to clindamycin.

Study Limitations

As our study was ED-based and not population-based, results may differ for patients who are treated in an outpatient clinic or private office setting. The data were collected from existing patient medical records, so some important clinical or historical information may have been missed. This study did not analyze the total number of patients with all types of skin infections, as we only performed cultures in those with abscesses. Our data were representative of the patient group in whom cultures were obtained and who had a specific type of skin infection. This raises the possibility of a selection bias that may have affected the overall antibiotic susceptibilities. We also lacked follow-up data on patients discharged from the ED, some of whom might have re-presented later at the same or a different institution with concurrent or subsequent infections. Finally, our study examined MRSA presence among our specific hospital population and therefore should not be extrapolated to other populations or geographic areas.

In summary, MRSA is common in pediatric patients with cellulitis and skin abscesses. Factors associated with MRSA infection include history of previous skin infection, exposure to contacts with skin infection, reported history of an insect bite, specific body site affected, and good health status without chronic conditions or recent hospitalizations. Clinicians need to be aware of the incidence of MRSA infection and its associated factors when treating pediatric patients presenting to the ED. Further research might focus on prospective multicenter studies of pediatric patients with skin infection to assess the incidence of MRSA nationwide and to confirm the generalizability of these or other risk factors.

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