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Methicillin-Resistant *Staphylococcus aureus* in Patients With Congenital Heart Disease in the Pediatric Intensive Care Unit

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Abstract

Background—Methicillin-resistant *Staphylococcus aureus* (MRSA) colonization has been recognized as a significant problem among hospitalized patients. Available data about prevalence of MRSA among children with congenital heart disease (CHD) are minimal. The aim of the study was to determine the prevalence of MRSA colonization and to identify risk factors for MRSA colonization among children <19 years old with CHD admitted to a pediatric intensive care unit (PICU).

Methods—Admission and weekly MRSA nasal surveillance testing was performed, and patients were stratified into six risk groups based on the Risk Adjustment for Congenital Heart Surgery-1 Method. The MRSA-colonized children were compared to the MRSA noncolonized children.

Results—During the 3-year study period, there were 372 admissions of children with CHD to the PICU. Of the 372, 72 (19.4%) had no surveillance cultures performed or had no prior history of MRSA and were excluded from further analysis. Of the remaining 300 admissions, 29 (9.7%) (263 individual children) were found to be colonized. The mean age of the 263 children when first admitted to the PICU was 3.29 years (range 0.03–18.30, median 0.66). Age distribution was not significantly different between the colonized and noncolonized groups ($P = .236$). Gender ($P = .667$), race ($P = .837$), and CHD complexity ($P = .395$) were not significantly associated with colonization. The odds of being colonized if previously hospitalized were 4.42 times greater than if not previously hospitalized (95% confidence interval 1.89, 10.34).

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Conclusion—Routine MRSA surveillance should be performed in patients with CHD to identify colonized patients.

Keywords

congenital heart disease; MRSA colonization; surveillance cultures

Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) continues to be an increasingly important cause of morbidity and mortality among patients in the United States and worldwide.¹ However, the majority of published data originate from studies conducted in adults, and only a few studies have focused on MRSA epidemiology in children.^{1–3} Moreover, there are sparse data describing the prevalence of MRSA colonization among children with congenital heart disease (CHD).

Most children with CHD now survive well into adulthood,⁴ and these children usually have multiple interactions with the health care system, especially those with more complex CHD. These interactions include hospitalizations for cardiac catheterization and surgery, often requiring admission to the pediatric intensive care unit (PICU). Hospitalization within the previous 12 months is a reported independent risk factor for MRSA colonization among adults.⁵ Gerber et al reported in a 6-year study of the incidence of *S aureus* infections among hospitalized children that 30% of patients admitted with *S aureus* infection had at least one complex chronic condition and 9% had a cardiac condition, although the details of these cardiac conditions were not reported.¹

Multidrug-resistant organisms, including MRSA, have been traditionally associated with the health care contact and the use of broad-spectrum antibiotics. However, a recent study showed increased prevalence (6%) of community-associated (CA-) MRSA colonization among patients admitted to the PICU.³

The objective of our study was to describe the prevalence of and risk factors for MRSA colonization among children with CHD admitted to the PICU.

Materials and Methods

We conducted a retrospective chart review of all children admitted to the PICU at Wolfson Children's Hospital (WCH) in Jacksonville, Florida between April 1, 2008, and March 31, 2011, with a history of CHD. The WCH is a 184-bed tertiary care children's hospital that serves north Florida and southeast Georgia. The 20-bed PICU annually admits an average of 1,000 medical and surgical patients (which include cardiac, orthopedic, and neurosurgical patients). All patients are admitted to single patient rooms. The study was approved by the institutional review boards of the University of Florida and WCH.

Medical records were reviewed for age, gender, CHD diagnosis, reason for admission to the PICU, length of stay (LOS) in the PICU, the number of previous hospitalizations, antibiotic use, and systemic corticosteroid use during the study period. In case of multiple admissions,

only the age at first admission was used for analysis. The patients who were admitted postcardiac surgery were stratified into six risk categories based on the Risk Adjustment for Congenital Heart Surgery 1 (RACHS-1).^{6,7} To describe the characteristics of the patients' prior hospitalizations, two authors reviewed the electronic medical records and gathered information on the use of antibiotics, whether the patient was admitted to the PICU, and was any surgical procedure performed during the hospitalization.

Starting from April 1, 2008, all children admitted to the PICU who had no known history of MRSA colonization or infection had nasal MRSA surveillance testing performed upon admission. These nasal swabs were collected by the PICU nurses. Patients who were not MRSA colonized on admission had weekly MRSA surveillance testing performed until they either tested positive or were discharged from the PICU. Patients with a previous history of MRSA colonization or infection were assumed to be MRSA colonized⁸; they were not tested for MRSA colonization and were immediately placed in isolation for the duration of their hospitalization. Any patient who had either an admission or weekly surveillance test positive for MRSA was immediately placed on contact isolation. There was no attempt to perform decolonization of MRSA for any patient who was identified as colonized.

Initially, MRSA identification was performed using a chromogenic media culture method (BBL CHROMAgarMRSA, Becton-Dickinson and Co, New Jersey) in accordance with manufacturer instructions.⁹ After April 2010, we used a real-time polymerase chain reaction (PCR) technique using Xpert MRSA that is run on the Gene Xpert system (Cepheid, Sunnyvale, California) according to manufacturers' instructions.¹⁰ The MRSA-colonized children were compared to the MRSA noncolonized children.

Statistical Methods

All analyses were run using SAS Version 9.3 for Windows (SAS Institute Inc, Cary, North Carolina). Categorical variables were described using counts and percentages and analyzed using chi-square tests or Fisher exact tests, when the estimated counts were less than five. Continuous variables were described using means, ranges, and medians and analyzed using the nonparametric Wilcoxon Rank-Sum tests. Bonferroni adjustment for multiple comparisons was applied when necessary. Odds ratios, along with 95% confidence intervals (CI), were extracted from logistic regressions. For the analysis of the prior hospitalizations, to take into account the missing information, log-rank tests were used to estimate the distribution of prior admissions with antibiotic use, ICU admission, and surgery, respectively. The patients with missing information were considered the censored observations.

Cox proportional hazards model analysis was used to determine the effect of antibiotic and steroid use on the MRSA colonization status.

Results

During the 3-year study period, there were a total of 2618 admissions (for 2281 children) to the PICU, of which 372 (14.2%) admissions were for 320 children with a history of CHD. There is no cardiac ICU; therefore all postsurgical patients are admitted to the general PICU.

Among the children with CHD, 72 (19.4%) admissions (in 69 individual patients) with no prior history of MRSA colonization were missed and not tested for MRSA colonization on admission. These 72 admissions were excluded from further analysis. The remaining 300 admissions were for 263 individual patients who were included in the analysis (Table 1). Of the 300 admissions, 29 (9.7%) were considered colonized (22 individual patients): 11 (3.7%) were newly identified by surveillance testing, 16 (5.3%) had prior history of MRSA colonization or infection, and 2 (0.7%) were identified by nonsurveillance clinical testing (both these patients had surveillance testing done on admission that was negative). There were no MRSA infections in patients with CHD admitted to the PICU during the study period. The prevalence of MRSA among all the patients admitted to the PICU during the study period was 15.8%.

The two clinical nonsurveillance positive cultures for MRSA (one each from the conjunctival sac and an incision wound site) were not treated by the clinicians and were considered to be colonization rather than infection for analysis.

Of the 300 admissions for patients with a history of CHD, 209 (69.7%) were postcardiac surgery and 91 (30.3%) were admissions for patients with a history of CHD who were being admitted to the PICU for nonsurgical management. Of the 209 patients who had surgery, 20 (9.6%) were found to have MRSA colonization, while 9 (9.9%) of the 91 who had no surgery were MRSA colonized ($P = .931$). Table 2 shows the prevalence of MRSA among the 209 postsurgical patients stratified by the six RACHS-1 risk categories.

The mean age of the 263 children with CHD at their first admission to the PICU (30 had multiple admissions during the study period) was 3.29 years (range = 0.03 to 18.66 years, median = 0.66 years). Table 1 shows the demographic characteristics of our patient population. Age distribution was not significantly different between the MRSA-colonized and noncolonized groups ($P = .407$, Wilcoxon Rank-Sum Test). Gender ($P = .667$, Chi-square), race ($P = .837$, chi-square), and CHD RACHS-1 category ($P = .383$, Fisher exact test) were also not significantly associated with colonization status.

Of the 122 admissions who had previous hospitalizations, 21 (17.2%) were found to have MRSA colonization, while eight (4.5%) of the 178 who had no previous hospitalizations were MRSA colonized. The odds of being colonized if previously hospitalized were 4.42 times greater than if not previously hospitalized (95% CI: 1.89, 10.34). The 122 admissions with prior hospitalizations represent 106 unique patients (18 colonized and 88 noncolonized). Medical records were only available going back ten years for these patients.

Of the 88 unique patients in the noncolonized group, 17 (19.3%) had completely missing (9 patients) or partially missing (8 patients) information about antibiotic use, surgery, or admission to the ICU, during their prior admissions. None of the 18 patients in the colonized group had missing information.

Of the 71 patients from the noncolonized group with complete information about antibiotic use, 54 (76.1%) had at least one type of antibiotic administered compared to 14 (77.8%) in the colonized group ($P = 1.000$, Fisher exact test). In all, 51 (71.8%) in the noncolonized group and 11 (61.1%) in the colonized group had at least one ICU admission ($P = .377$, chi-

square). Forty (56.3%) patients in the noncolonized group and 12 (66.7%) in the colonized group had at least one surgery ($P = .427$, chi-square).

The estimated median for the proportion of prior hospitalizations with antibiotic use was 76.4% (95% CI: 50.0%, 100.0%) for the colonized group versus 100% (95% CI: 60.0%, 100.0%) for the noncolonized group ($P = 0.552$).

The estimated median for the proportion of prior hospitalizations with ICU admission was 100.0% (95% CI 0%, 100.0%) for the colonized group versus 100% (95% CI: 66.7%, 100.0%) for the noncolonized group ($P = .508$). The estimated median for the proportion of prior hospitalizations with surgery was 50.0% (95% CI 0%, 100.0%) for the colonized group versus 50% (95% CI: 33.3%, 100.0%) for the noncolonized group ($P = .722$).

Of the 29 MRSA-colonized admissions, 13 (44.2%) were patients newly identified for the first time as MRSA colonized during the PICU admission. These 13 admissions were analyzed for the effect of antibiotic and steroid use on becoming MRSA colonized. In all, nine (69.2%) of the 13 newly colonized admissions and 241 (89%) of the 271 noncolonized admissions received antibiotics ($P = .056$, Fisher exact test), approaching statistical significance. However, in children who received antibiotics and steroids, using a Cox proportional hazards model analysis and controlling for steroids, the use of antibiotics had a protective effect, reducing the risk of being MRSA colonized by 81% (hazard ratio = 0.189, 95% CI: 0.045, 0.784).

Comment

Staphylococcus aureus carriage is a well-known risk factor for infection.^{11,12} One report estimated the relative risk of surgical site infections associated with nasal colonization, compared to no colonization, to be more than eight times higher.¹³ Safdar and Bradley performed a systematic review and estimated that the risk of infection following colonization with MRSA was fourfold higher when compared with methicillin-susceptible *Saureus*.^{12,14}

Routine surveillance for MRSA and other important antibiotic-resistant pathogens is often an important element of effective infection control programs.¹² Holzmann-Pazgal reported that admission and weekly active surveillance culturing appeared to be an effective tool to decrease the spread of MRSA in a PICU, independent of improving hand hygiene compliance.¹⁵

One of the goals of this study was to determine the prevalence of MRSA among patients with CHD who are admitted to the PICU. We believe that identification and isolation of these patients were important to prevent the spread of MRSA among all patients admitted to the PICU. The results of our study demonstrated that among this group of patients with CHD who have increased contact with the health care system, the prevalence of MRSA colonization (9.5%) was higher than the 6% rate reported by Milstone et al in a study done on a general PICU population.³ Currently, MRSA accounts for more than 60% of staphylococcal infections in the ICU,¹² and the most common type of infections with MRSA, especially CA-MRSA, are skin and soft tissue infections.¹⁶ Interestingly, there were

no patients with MRSA infection in our study; however, all of our surgical cardiac patients receive prophylactic antibiotic therapy with vancomycin that covers MRSA.

Our results also demonstrated that when comparing patients who became MRSA colonized to those who were not, the use of antibiotics had a protective effect, reducing the risk of being affected by 81%, when controlling for steroid use in patients who received both antibiotics and steroids. We do not have an explanation for this finding, and considering that only a small number of patients became MRSA colonized while admitted to the PICU this result should be interpreted with caution and further research is necessary to address this issue. In published studies, patients who were MRSA colonized tended to be younger.³ In our patients, we found that age, gender, and RACHS-1 risk category were not predictors of MRSA colonization. We also found that prior hospitalization was associated with a fourfold higher likelihood of MRSA colonization. Further characterization of the previous hospitalizations demonstrated no significant difference in the use of antibiotics, being admitted to the PICU, or having a surgical procedure between those patients who were MRSA colonized and those who were not.

Our retrospective data collection and the fact that almost one-fifth of the patients admitted to the PICU with CHD were excluded from analysis because the opportunity to perform baseline MRSA surveillance was missed are other limitations of our study. However, there were no significant differences in the mean age ($P = .06$), gender ($P = .5$), and ethnicity ($P = .34$) between the patients who were included and those excluded from the analysis (data not shown).

In view of the high prevalence of MRSA colonization among children with CHD in our study, we conclude that our findings support the routine surveillance for MRSA in such children upon admission to the PICU, especially in those patients with a history of prior hospitalizations. This should help to prevent possible inadvertent transmission to noncolonized hospitalized patients by identifying the colonized patients and placing them in appropriate isolation. Since we did not attempt to decolonize patients identified with MRSA, further studies will need to be conducted to determine whether there is a benefit of decolonization to prevent acquisition and transmission of MRSA among patients with CHD admitted to the PICU.

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Table 1

Characteristics of Patients With CHD Admitted to the PICU.

Characteristic	Unique Patients, n = 263 (%)	MRSA Colonized, n = 22 (%)	No MRSA, n = 241 (%)
Mean age, years (range)	3.29 (0.03–18.66)	2.56 (0.02–17.1)	3.41 (0.003–18.66)
<28 days old	30 (11.4)	3 (13.6)	27 (11.2)
28–364 days	116 (44.1)	9 (40.9)	107 (44.4)
1–5 years	55 (20.9)	7 (31.8)	48 (19.9)
5–10 years	28 (10.6)	1 (4.5)	27 (11.2)
10 years	34 (12.9)	2 (9.0)	32 (13.3)
Gender (%)			
Male	143 (54)	11 (50)	132 (55)
Female	120 (46)	11 (50)	109 (45)
Race (%)			
Caucasian	162 (62)	14 (64)	148 (61)
Non-caucasian	101 (38)	8 (36)	93 (39)

Abbreviations: CHD, congenital heart disease; MRSA, methicillin-resistant *Staphylococcus aureus*; PICU, pediatric intensive care unit.

Table 2

The MRSA Prevalence Among Postcardiac Surgery Patients Stratified by RACHS-1 Risk Category.

RACHS-1 Category	All Surgical Admissions, n = 209 (%)	MRSA Colonized, n = 20 (%)	No MRSA, n = 189 (%)
1	29 (13.9)	1 (5)	28 (14.8)
2	102 (48.8)	10 (50)	92 (48.7)
3	60 (28.7)	7 (35)	53 (28.0)
4	9 (4.3)	0 (0)	9 (4.8)
5	1 (0.5)	0 (0)	1 (0.5)
6	8 (3.8)	2 (10)	6 (3.2)

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; RACHS-1, risk adjustment for congenital heart surgery-1.