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Resistance to Methicillin and Other Antimicrobials Among Community-Acquired and Nosocomial *Staphylococcus aureus* Strains in a Pediatric Teaching Hospital in Salvador, Northeast Brazil

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To report the frequency of methicillin-resistant *Staphylococcus aureus* (MRSA) infection and to compare the antimicrobial resistance patterns between community-acquired (CA) and nosocomial (NI) strains stratified for resistance to methicillin, this retrospective study on patients under 20 years of age was conducted from April 1995 to December 2005 in a pediatric teaching hospital in Salvador, Brazil. Of 308 *S. aureus* strains isolated, 185 (60.1%) were reviewed, out of which 125 (67.6%) and 55 (29.7%) had CA or NI infection, respectively, and 5 were defined as colonization. Out of the nine patients with MRSA initially diagnosed as CA, three were excluded from the analysis because of report of hospitalization during the previous year. Resistance to methicillin was more frequent among NI (30.9% vs. 4.9%, $p < 0.001$). Resistance to other antimicrobials was more common among NI-MRSA compared with CA-MRSA. Although at a low rate, CA-MRSA has occurred among children, in this region.

Introduction

Staphylococcus aureus is a major human pathogen, and the development of new antibiotic resistance has imposed an additional challenge on physicians.[10] The increase in methicillin-resistant *S. aureus* (MRSA) community-acquired (CA) infections affecting healthy children has been reported worldwide since 1990s.[9] Nonetheless, there are no previously published data regarding the frequency of MRSA childhood infection in Northeast Brazil. The aims of this study were to report the frequency of MRSA infection and to compare the antimicrobial resistance patterns between CA and nosocomial (NI) strains stratified for resistance to methicillin.

Materials and Methods

This was a retrospective study. All *S. aureus* strains isolated from patients under 20 years of age between April 1995 and December 2005 were identified by reviewing the books of results of both Bacteriology Laboratories at the university hospital (Federal University of Bahia) in Salvador, Northeast Brazil. The medical records were reviewed, and the isolates were classified as colonization, NI, or CA infection. Colonization was considered when there was no sign or symptom,[14] and such strains were excluded. Infections were classified as NI if they met the 1988 Centers for Disease Control and Prevention (CDC) criteria for NI.[6] *S. aureus* was identified by routine procedures, including catalase and coagulase tests. Antimicrobial resistance was searched by the disk-diffusion method according to the Clinical and Laboratory Standards Institute,[4] and those results were collected. In order to search resistance to methicillin, a 1 μg oxacillin disk was applied to Mueller–Hinton agar containing 5% sodium chloride and incubated at 37°C. CA-MRSA infection was defined according to the CDC definition reported in February 2005[9]: identification of MRSA in a patient with signs and symptoms of infection, either in the outpatient setting or within 48 hours after admission to a hospital, with no history of MRSA infection or colonization, no history of admission to a hospital or a nursing home, surgery, dialysis within 1 year of the MRSA culture date, and absence of permanent indwelling catheter or percutaneous medical device at the time of culture. Statistical analysis was performed with the softwares EPI INFO 6 (EPI6) and Statistical Package for Social Science (SPSS, version 9.0). Proportions were assessed by the Pearson chi-square or Fisher exact test, as appropriate. Statistical significance was attributed when $p < 0.05$. The Ethics Committee of the university hospital approved this study.

Results

During the study period, 308 strains of *S. aureus* were isolated. Of those, 185 (60.1%) episodes of 176 patients were

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reviewed, out of which 125 (67.6%) and 55 (29.7%) had CA or NI infection, respectively, according to the 1988 CDC criteria for NI.[6] The selection of the 185 episodes was based solely on the accessibility of the medical records to be reviewed in order to collect clinical data. Five (2.7%) strains were classified as colonization and were excluded. Table 1 presents the frequency of antimicrobial resistance among NI, CA, methicillin-susceptible *S. aureus* (MSSA), and MRSA strains. Resistance to methicillin, clindamycin, rifampin, ciprofloxacin, erythromycin, and gentamicin was significantly higher among NI strains, and resistance to penicillin was significantly higher among CA strains. Among NI strains, the frequency of resistance to several antimicrobials was statistically higher among MRSA. On the other hand, among CA strains, the antimicrobial resistance rates were statistically similar when MRSA and MSSA strains were compared.

Out of the nine patients with MRSA initially diagnosed as CA, three were excluded from the analysis because of report of hospitalization during the previous year. Out of 122 CA *S. aureus* strains studied, MRSA was detected in 6 (4.9%, 95% confidence interval 2.0–10.0%). None of the studied strains was resistant to vancomycin. Resistance to chloramphenicol and tetracycline was not tested.

Four of the six patients with CA-MRSA were females and two were newborns. The other ages were 5.4 months old ($n = 2$), 3.1 years old, and 11 years old. *S. aureus* was isolated from blood ($n = 5$) and from abscess of lymph node ($n = 1$), in the years 1996 ($n = 2$), 2002 ($n = 2$), 2004 ($n = 1$), and 2005 ($n = 1$). The diagnoses were pneumonia ($n = 3$), bacterial skin infection ($n = 2$), and lymphadenitis ($n = 1$). Three patients were severely malnourished. None of them reported previous burn or contact with health professionals.

Discussion

From the results reported herein, it is possible to state that CA-MRSA has occurred among children in our region (Table 1). CA-MRSA has been detected at alarming scale in pediatric hospitals in other regions, like Houston, Texas, where more than 70% of CA *S. aureus* isolated since 2001 were methicillin resistant.[11] In comparison with such data, the frequency in this study was low (4.9%, 95% confidence interval 2.0–10.0%), but it is already a reality. It has been recognized that CA-MRSA is usually resistant to fewer antimicrobials and it is epidemiologically similar to community-acquired MSSA (CA-MSSA), and not to the multiresistant nosocomial-acquired MRSA (NI-MRSA).[10] By analyzing data shown in Table 1, it is possible to observe that the frequency of resistance to other antimicrobials was lower among CA-MRSA compared with NI-MRSA. It was described that most of CA-MRSA strains contain a unique genetic element called SCC*mec* type IV that differs from NI-MRSA by the absence of non-β-lactam genetic-resistance determinants and its smaller size facilitates its spread among *S. aureus* strains.[5] Afterward, SCC*mec* types V and VI associated with CA infection were also identified.[3,12]

In a previous study conducted at another hospital in Salvador, the overall prevalence of MRSA was 28% and the occurrence of CA-MRSA was reported.[1] However, those authors did not inform the patients' age, the specific rate of CA-MRSA, nor the used criteria for defining CA-MRSA. *S. aureus* carriage was evaluated within 6 hours from hospital

Table 1. Frequency of Antimicrobial Resistance Among Community-Acquired and Nosocomial Strains of *Staphylococcus aureus*, in a Pediatric Teaching Hospital, 1995–2005, Salvador, Northeast Brazil

	Type of infection			*Community-acquired* S. aureus *strains*			*Nosocomial* S. aureus *strains*		
Antimicrobial	*Community-acquired*	*Nosocomial*	p-*value*	*MRSA*	*MSSA*	p-*value*	*MRSA*	*MSSA*	p-*value*
Penicillin	95.7 (111/116)	84.6 (44/52)	0.02	100.0 (6/6)	95.5 (105/110)	1.0	100.0 (17/17)	77.1 (27/35)	0.04
Methicillin[a]	4.9 (6/122)	30.9 (17/55)	<0.001	–	–	–	–	–	–
SMX-TMP	16.8 (17/101)	30.4 (14/46)	0.08	20.0 (1/5)	16.7 (16/96)	1.0	54.5 (6/11)	22.9 (8/35)	0.06
Clindamycin	16.0 (13/81)	36.7 (11/30)	0.02	25.0 (1/4)	15.6 (12/77)	0.5	37.5 (3/8)	36.4 (8/22)	1.0
Rifampin	0 (0/108)	6.3 (3/48)	0.03	0 (0/5)	0 (0/103)	–	20.0 (3/15)	0 (0/33)	0.03
Ciprofloxacin	4.4 (5/113)	19.6 (9/46)	0.004	0 (0/5)	4.6 (5/108)	1.0	61.5 (8/13)	3.0 (1/33)	<0.001
Erythromycin	38.6 (44/114)	63.5 (33/52)	0.004	33.3 (2/6)	38.9 (42/108)	1.0	80.0 (12/15)	56.8 (22/37)	0.2
Gentamicin	9.5 (11/116)	21.2 (11/52)	0.04	16.7 (1/6)	9.1 (10/110)	0.5	40.0 (6/15)	13.5 (5/37)	0.06
Amikacin	6.5 (6/92)	15.2 (7/46)	0.1	20.0 (1/5)	5.7 (5/87)	0.3	40.0 (6/15)	3.2 (1/31)	0.003

Results are reported in % (*n*/*N*).
[a]Resistance to methicillin was searched by using a 1 μg oxacillin disk.
MRSA = methicillin-resistant *S. aureus*; MSSA = methicillin-susceptible *S. aureus*.

admission among children younger than 5 years with respiratory tract infection and meningitis in Goiânia, Central Brazil, and the reported MRSA rate was 1%.[8] Those authors did not use the up-to-date CDC criteria for defining CA-MRSA,[9] but they state that no genuine CA-MRSA strain was found since the MRSA isolates were resistant to antimicrobials other than β-lactam antibiotics. MRSA was detected in five patients with CA *S. aureus* bacteremia in another study (mean age of patients 46 years) conducted in Goiânia, Central Brazil, but all five patients had previous follow-up in healthcare facilities due to chronic diseases.[7] Therefore, those MRSA strains were not genuine CA according to CDC definition.[9] In Recife, another city in Northeast Brazil, MRSA carriage was detected in 13% of patients over 12 years of age during the first 48 hours following admission to the Intensive Care Unit and a significant association was established between previous hospitalization and the presence of MRSA.[2] So, one can infer that several of those MRSA were not really CA strains. Evidence has been documented that the international CA-MRSA clones are present at Rio de Janeiro and Porto Alegre, two other cities in South Brazil.[13] The evidence presented herein supports the occurrence of genuine CA-MRSA among children in Salvador, Northeast Brazil, according to CDC 2005 definition.[9] Therefore, the authors speculate about the possible circulation of CA-MRSA clones throughout Brazil.

The limitations of this study must be emphasized. Vancomycin resistance was searched by the disk-diffusion method, and resistance to chloramphenicol and tetracycline was not tested. The last procedure was not included in the routine of the bacteriology laboratory during the study period. Therefore, such information could not be found as this was a retrospective study. All staphylococcal isolates for which vancomycin zone diameters are 14 mm or less should be tested by a reference minimum inhibitory concentration (MIC) methods.[4]

The significant lower rate of resistance to penicillin among NI *S. aureus* strains is noteworthy (84.6% vs. 95.7%, $p = 0.02$). The authors question if this finding may be attributable to a circulating clone in the hospital. Further, prospective evaluation is needed in order to clarify this finding. Continuous surveillance of CA *S. aureus* infection is recommended in order to evaluate the empiric antimicrobial treatment that is appropriate in each region.[10]

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