Temporal Evolution of the Prevalence of Methicillin-Resistant *Staphylococcus aureus* in a Tertiary Hospital in Bahia, Brazil. A Nine-Year Evaluation Study

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Infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) have become an increasing problem in Brazilian hospitals within the last years. In Bahia, there is scarce information on the epidemiological characteristics of MRSA infections and their determinants. The objective of this study was to evaluate the temporal evolution of MRSA infections in a private, tertiary hospital, in Salvador, the capital of the state of Bahia. We reviewed the microbiological records of bacterial isolates from the Hospital Espanhol, a 300 bed, general hospital, in Salvador. We analyzed the frequency of positive cultures for *S. aureus* during the last nine years, the prevalence of MRSA, and the spatial distribution of the isolates in the hospital. We also evaluated the temporal evolution of MRSA during the study period. Seven-hundred-ten cultures were positive for *S. aureus* from 1996 through 2004. The prevalence of MRSA was 28%. The intensive care unit (59%), the hemodyalisis unit (43%), and the infectious diseases unit (34%) presented with significantly higher prevalence of MRSA, when compared to the remaining clinics of the hospital. We detected a significant increase of MRSA isolation among patients with nosocomial infections, over time (P<0.0001). MRSA isolates were highly resistant to alternative drugs (clyndamicin, erythromycin, co-trimexazole, levofloxacin), reinforcing the likelihood of nosocomial acquisition of the pathogen. The overall prevalence of MRSA in the hospital has remained relatively stable within the last nine years, but there was a significant trend forincreasing nosocomial acquisition of MRSA over time, which is even higher for patients attended in intensive care units, HDU, or IDU.

Key Words: *Staphylococcus aureus*, MRSA, bacterial resistance.

Staphylococcus aureus is a very resilient bacteria, which can survive under very unfavorable conditions. Resistance of *S. aureus* to methicillin/oxacilin, the first choice drugs for treating infections caused by this pathogen is becoming a common finding in most parts of the world. In a pediatric hospital, in Houston, USA, 74% of isolated community-acquired *S. aureus* strains in 2001 were resistant to methicillin [1-3]. In addition, resistance to drugs considered of choice to treat methicillin-resistant *S. aureus* (MRSA) is already recognized, and tends to become a major threat for patients infected by these strains [4,5].

In Brazil, MRSA has often been described in several settings, but there is a great variation in the prevalence of this pathogen, according to the region, or even to the hospital in which the study was conducted [6]. The importance of community-acquired strains of MRSA has been assessed by various authors, as has the impact of MRSA on the mortality of patients infected by resistant strains of *S. aureus* [3,7,8]. However, there is still scarce information on the real importance of MRSA infections in Bahia. Most of the reports on prevalence and risk factors for acquisition of MRSA in Brazil are restricted to other regions and institutions of the country. A large number of papers have focused on the characterization of MRSA, its epidemiological pattern, and prevalence in different hospitals in other parts of the country [6,9-12]. There are many pending questions on MRSA infections in Brazil, its importance as a nosocomial pathogen, impact on mortality, and the role of community-acquired infections caused by this pathogen.

We have observed an increasing number of MRSA infections in different hospitals, in Salvador, the capital and largest city of Bahia state. The lack of information on the actual prevalence of MRSA infections, its importance as a nosocomial pathogen, its prevalence in the community and other fundamental data are not available in our region. Knowing the importance of such infections, and the trends over time can be fundamental for designing strategies for the control and prevention of its transmission.

We examined the evolution of *S. aureus* infections over time, in a tertiary hospital, in Bahia, Brazil. We evaluated the prevalence and characteristics of MRSA during a 10-year period, for patients admitted to a 300-bed, tertiary private hospital, in Salvador.

Material and Methods

Setting

The study was conducted at the Hospital Espanhol (HE), a 300 bed, private tertiary hospital, located in Salvador, Bahia. It is a private hospital, but due to its philanthropic profile, it also receives patients from the public health system (Sistema Único de Saúde - SUS). The hospital has a 25 bed-intensive

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care cnit (ICU), a 10 bed semi-ICU, and the main clinical specialties, including oncology, and infectious disease clinics. The HE also had a specific clinic for infectious diseases, which was closed in 2003, although the hospital continues to admit such patients, but without a specific facility for receiving them. It also performs transplantation (mostly kidney transplantation), and has hemodialysis and neonatal units. The hospital's Infection Control Committee (ICC) was created in 1992.

Study design

This was a retrospective study. The ICC keeps a database with all microbiological reports recorded during the last 9 years. All positive cultures are reported to ICC and then entered into a database, which contains information on the site of isolation, date, microorganism that was isolated, sensitivity profile to the main antibiotics, and whether the case was acquired during hospitalization (nosocomial infection) or not. For analysis purposes, we recorded the cultures positive for *S. aureus* from 1996 to 2004. The data were analyzed by using the software Epi-Info version 6.0.

Results

A total of 6,315 positive cultures were detected during the study period. Within this sample 715 (11.3%) cultures were positive for *S. aureus*. The main topographies for bacterial isolation were the blood stream (38%), skin and surgical wound infections (20%), central venous catheter (4.5%), and 4.2% from the remains of the umbilical cord in neonates. Hospital acquired infections contributed to 59% of the isolates. The overall prevalence of MRSA was 28% (202/715 cultures). Figure 1 shows the distribution of positive cultures for *S. aureus* as well as the proportion of MRSA, over time.

Table 1 shows the distribution of positive cultures for *S. aureus* by hospital area. A total of 112 (16%) positive cultures were isolated from patients attended at the hospital emergency room, while 106 (15.2%) originated from patients admitted to the ICU, and 94 (14.9%) from the neonatal ICU. The infectious diseases ward (closed in 2002) had 40 (5.7%) of the total positive cultures, while hemodialysis patients provided 15 (2.1%) of the positive cultures. We found that the ICU had significantly more MRSA cultures than non-critical areas (59.4% *versus* 22.3%, respectively, relative risk (RR) = 2.6; 95% confidence interval (CI): 2.10 – 3.23, P<0.00001). In addition, the adult ICU was much more likely to have MRSA positive cultures than the neonatal ICU (59.9% and 18.5%, respectively, RR = 3.22; 95% CI: 1.89 – 5.49, P<0.00001). Also, the prevalence of MRSA was 35% in the Infectious Diseases Unit, and 43% among patients from the Hemodyalisis Unit. There were no significant differences in the prevalence of MRSA in these three units.

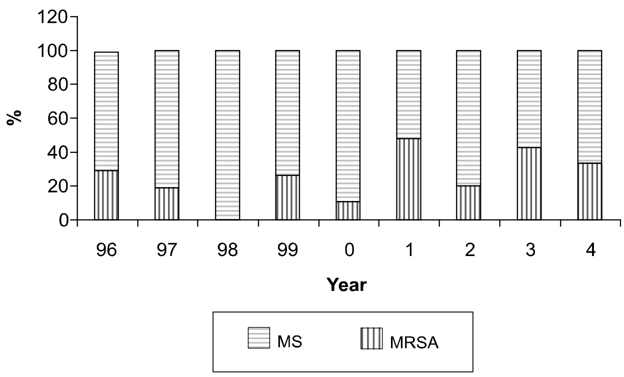
Table1. Spatial distribution of *Staphylococcus aureus*-positive cultures, according to their sensitivity profile

Area	Positive cultures(N)	MRSA% (%)	Total cases
ICU	106	59.4	14.9
Neonatal Unit	94	18.5	13.2
Emergency room	112	3.6	15.8
Infectious diseases	40	35	5.6
Hemodyalisis unit	15	43	2.1
Other clinics	343	18.3	48.3
Total	710	-	28.3

ICU = intensive care unit.

As expected, there was a strongly significant association between MRSA-positive cultures and nosocomial infections, (RR = 2.6; 95% CI: 2.17 – 3.13, P<0.00001). Nevertheless, when we analyzed the temporal distribution of MRSA infections, we observed that there was not a trend over time for increasing the prevalence of such infections. Comparing the periods of 1996-1999 and 2000-2004 the proportion of cases of MRSA was similar (OR=0.89; 95% CI: 0.43 – 0.84, Yates corrected). However, this was not true for the proportion of MRSA-positive cultures among patients with nosocomial infections. A significantly higher proportion of nosocomial infections due to MRSA was detected within the last five years, compared to the 1996-1999 period: the OR for acquiring a MRSA infection not related to hospitalization decreased from 0.50 (95% CI: 0.31 – 0.82, P=0.01) to 0.30 (95% CI: 0.13 – 0.30, P<0.0001). The comparison of the two periods confirmed the trend for decreasing the risk of non-nosocomial MRSA infections (OR= 0.16; 95% CI: 0.11–0.25, P=0.002, Mantel-Haensel). Conversely, this fact becomes even more clear when we look at the chances of a patient be infected by *S. aureus* not related to hospitalization, within the last five years (OR=1.92; 95% CI: 1.48 – 2.49, P<0.0001), compared to the first four years of the period covered by this study. In addition, when we analyzed the risk ratio for a positive MRSA culture among patients attended at the emergency room, within the two time periods, we detected no significant difference between the RR for the first four years of study (RR=0.24; 95% CI: 0.04 – 0.29) and the second one (RR=0.04; 95% CI: 0.01 – 0.3, P value for comparison of the periods: 0.1)

Figure 1.



The analysis of sensitivity of *S. aureus* to other antibiotics considered as alternative choices for treating such infections revealed a high level of cross-resistance to these drugs and to methicillin. The RR for resistance to erythromycin if the isolated agent was a MRSA was 4.95 (95% CI:3.75–6.53, P<0.0001), for clindamycin it was 21.06 (95% CI: 13.53–32.06, P=0.0001), levofloxacin 5.3 (95% CI: 4.34–6.41, P<0.0001), gentamicin 14.74 (10.07–21.56, P<0.0001), and amikacin, 9.01 (95% CI: 5.56–14.61, P<0.0001). This fact reinforces the higher risk found for acquisition of MRSA within the hospital.

Discussion

The prevalence of MRSA in hospitalized patients, admitted to HE, in Salvador has been increasing over time. A total of 201 (28%) *S. aureus*-positive cultures were resistant to methicillin/oxacillin. However, although we found strong evidence that MRSA is increasing as a nosocomial pathogen, this was not true for the overall prevalence of infection caused by that agent. The likely explanation for this discrepancy is an increasing likelihood of acquisition of MRSA for hospitalized patients, due to a greater circulation of MRSA strains within the hospital, associated with a relative decrease of introduction of this agent from the community. The decrease in prevalence of MRSA among patients attended at the emergency room, observed over time in this study supports this hypothesis. In addition, the finding of a strong relationship between resistance to methicillin and to drugs like clindamycin, erythromycin, gentamicin, and amikacin also reinforces that possibility. It is already recognized that community-acquired MRSAs are less likely to display cross-resistance to other drugs, while hospital-acquired strains behave in the opposite way [12,13].

It was not surprising to detect a greater risk for isolation of MRSA among patients admitted to the ICU. In addition, the higher prevalence found in HD units and in the infectious diseases unit also were expected. There is much evidence supporting the contention that such units are a major risk for acquiring bacterial infections caused by multi-resistant organisms, since these areas are the main location, in any hospital, for intensive use of antibiotics, leading to a strong selective pressure that results in an increasing prevalence of multi-resistant bacteria [14,15]. In our study, this seems to be clear when we compare the rates of MRSA for the different hospital areas. In the neonatal ICU, for instance, where the use of antibiotics is much less frequent, the rates of MRSA isolation were significantly lower, reinforcing the role of adult ICUs as a high-risk area for acquiring MRSA.

Many hypotheses have been proposed on the potential sources for MRSA dissemination in hospitals [16]. Besides the bacterial characteristics, which allow it to survive in diverse environments, the intensive use of antibiotics is considered one of the main reasons for the selection of MRSA. In addition, health professionals are considered as one of the main routes for transmission of MRSA within hospitals, serving as a transmitting vehicle from a patient infected by these agents and other, uninfected ones [17]. Thus, strict compliance with infection control committee recommendations is essential to contain the spreading of MRSA in hospitals, and even to block the carriage from one health institution to another [18]. Use of barrier measures, and hand washing are considered crucial to avoid the transmission of MRSA through health professionals to hospitalized patients. Also, the nasal colonization of health professionals by MRSA has been recognized as an efficient means to maintain endemic levels of MRSA in specific areas [19-23]. In the HE we performed an analysis of the nasal carriage of MRSA among health professionals, during the investigation of an outbreak in 2004 (unpublished data). An overall prevalence of 12% of nasal colonization by *S. aureus* was detected, and 7% of the people presenting positive cultures harbored an MRSA strain. Half of the MRSA-positive professionals were working in the ICU, during the investigation period. This fact lead us to concentrate our efforts for control of MRSA on ICU personnel, and to promote a search for nasal carriers among them, in order to control MRSA dissemination in that unit.

We found that there are some important factors associated with MRSA prevalence and evolution during the last 10 years in HE. The main current challenge for the ICC is to deal with the endemic levels of MRSA infections, trying to reduce them, and to control the spread of such strains to other hospital areas. Educational measures, isolation of positive cases, and optimizing antibiotic use probably are the best intervention procedures, in order to reach such goals.

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