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Original Article

Methicillin Resistance among Trinidadian Isolates of Community and Hospital Strains of *Staphylococcus aureus* and Their Patterns of Resistance to Non-β-Lactam Antibiotics

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SUMMARY: The prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) strains in Trinidad and the extent of their resistance to other antimicrobial agents in hospital-acquired and community-acquired infections were evaluated over a 2-year period. A total of 450 *S. aureus* strains were isolated from different patients. The prevalence of methicillin resistance among *S. aureus* strains was 9.8% (44/450). The proportion of MRSA isolated from hospital sources and community sources was 12.5% (38/305) and 4.1% (6/145), respectively ($P < 0.05$). The resistant rates of MRSA to the non-β-lactam antibiotics were as follows: 93.2% resistance to tetracycline, 68.2% to erythromycin, 61.4% to gentamicin, 45.5% to co-trimoxazole, and 20.5% to ciprofloxacin. No MRSA resistant to vancomycin was observed in this study. Study results showed significant increases in MRSA in hospital, 2% in 1995 to 12.5% in 1998 ($P < 0.05$), and community, 0% in 1995 to 4.1% in 1998 ($P < 0.05$). It has become apparent that infection control and surveillance initiatives must be focused now on the community in order to monitor and limit the spread of this new and expanding reservoir of MRSA.

INTRODUCTION

Staphylococcus aureus is the single most frequently encountered bacterial species in hospitals (1) and the most common etiological agent of hospital-acquired post-operative surgical wound infections (2,3). In the 1960s, methicillin-resistant *Staphylococcus aureus* (MRSA) strains first emerged as a major hospital-acquired pathogen, both in Europe (4), North America (5), and other parts of the world, and the emergence of this resistance correlates with the development of increasing resistance to other antimicrobial agents (6). Therefore, MRSA strains maybe resistant to several other classes of antimicrobial agents, including the quinolones, clindamycin, tetracyclines, erythromycin, trimethoprim-sulfamethoxazole as well as the aminoglycosides (7,8).

Several mechanisms for the methicillin resistance seen in *S. aureus* have been elucidated. The most important is production of a unique penicillin-binding protein (PBP) that has a low affinity for β-lactam drugs and whose effects are determined by several structural genes (*mecA*, *mecRI*, *mecI*) (9,10). Other known mechanisms of methicillin resistance are the production of the usual PBPs, but with modified affinities for the β-lactam drugs, and the hyperproduction of penicillinase enzyme (8).

MRSA strains can spread from infected patients to medical staff, who often become transient carriers (11). Infections with these organisms are life-threatening in immunocompromised patients, often difficult to manage, and problematic to eradicate. It is therefore of primary importance to decrease the prevalence of MRSA by measures such as rapid and reliable identification of the organisms along with their sensitivities to other antibiotics, isolation and treatment of patients and carriers, and strict adherence to hand washing practices by medical staff.

The objectives of this study were to determine the prevalence of Trinidadian strains of MRSA isolated from hospital practice and community practice and their antimicrobial resistance profiles.

MATERIALS AND METHODS

Between January 1, 1997 and December 31, 1998, we examined strains of *S. aureus* from various clinical sources in hospital and community practices in Trinidad for methicillin resistance. Specimens were derived from patients on the wards and from those attending outpatient clinics at the Eric Williams Medical Sciences Complex (EWMSC). The EWMSC is a 560-bed medical facility located in the northwest part of the country of Trinidad, which is the larger of the twin island Republic, Trinidad and Tobago, located about 11 km off the northern coast of Venezuela in South America. The population of the Republic is about 1.25 million. For purposes of this investigation, we did not differentiate between isolates from inpatients and outpatients; all isolates were classified as "hospital-practice". Specimens received from patients attending health care centers in the community and from those seen by general practitioners were classified as "community-practice" isolates. For purposes of gathering infection control surveillance data, other organisms and duplicates of clinically significant isolates were excluded from the hospital specimens that were received.

S. aureus strains were tested for resistance to methicillin on Mueller-Hinton agar (BBL Microbiology Systems, Cockeysville, Md.) via the disc diffusion method outlined by the National Committee for Clinical Laboratory Standards (NCCLS) (12) using a 1 μg oxacillin disc. Plates were

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incubated aerobically at 33-35°C for a full 24 h. Strains with zone sizes less than 10 mm were regarded as methicillin resistant. By the disc diffusion method specified by the NCCLS, MRSA isolates were tested against the following antibiotics and concentrations (in brackets): vancomycin (30 μg), ciprofloxacin (5 μg), gentamicin (10 μg), co-trimoxazole (trimethoprim-sulfamethoxazole) (25 μg), erythromycin (15 μg), and tetracycline (30 μg) (12). The MRSA control strain was *S. aureus* (ATCC 49476), obtained from the Caribbean Epidemiology Center (CAREC), a branch of the Pan American Health Organization/World Health Organization.

RESULTS

From the 15,922 specimens submitted to the EWMSC from clinical sources for microbiological investigations, a total of 450 (2.8%) strains of *S. aureus* were isolated during the study period (305 from hospital practice and 145 from community practice sources) (Table 1). The overall methicillin-resistant rate in *S. aureus* was 9.8% (44/450). The prevalence of methicillin resistance among *S. aureus* strains isolated from hospital and community patients was 12.5% and 4.1%, respectively. This difference was statistically significant ($P < 0.05$).

Table 1. Distribution of 450 *Staphylococcus aureus* strains isolated from hospital and community sources according to methicillin resistance, 1997-1998

Methicillin	No. of hospital isolates (%)	No. of community isolates (%)	Total (%)
Sensitive	267 (87.5)	139 (95.9)	406 (90.2)
Resistant	38 (12.5)	6 (4.1)	44 (9.8)
TOTAL	305 (100.0)	145 (100.0)	450 (100.0)

Hospital MRSA: 1995 vs 1998, $X^2 = 5.48$; $P < 0.05$.
Community MRSA: 1995 vs 1998, $X^2 = 5.39$; $P < 0.05$.

Table 2. Prevalence of resistance of 44 MRSA[1] strains to other antimicrobial agents, 1997-1998

Antimicrobial	No. of strains tested	No. of strains resistant (%)
Vancomycin	44	0
Tetracycline	44	41 (93.2)
Erythromycin	44	30 (68.2)
Gentamicin	44	27 (61.4)
Co-trimoxazole[2]	44	20 (45.5)
Ciprofloxacin	39	8 (20.5)

[1]MRSA=methicillin-resistant *Staphylococcus aureus*; [2]Co-trimoxazole= trimethoprim-sulfamethoxazole.

Table 3. Clinical Sources of MRSA[1] and MSSA[2] strains isolated at the EWMSC[3], 1997-1998

Source	MRSA		MSSA	
	No.	%	No.	%
Wounds	24	54.5	279	68.7
Urine	8	18.2	53	13.1
Lower Respiratory Tract (sputum)	5	11.4	26	6.4
Boils and abscesses	4	9.1	19	4.7
Blood	3	6.8	29	7.1
TOTAL	44	100.0	406	100.0

[1]MRSA=methicillin-resistant *Staphylococcus aureus*, [2]MSSA= methicillin-sensitive *Staphylococcus aureus*, [3]EWMSC=Eric Williams Medical Sciences Complex.

Table 2 shows the prevalence of resistance of MRSA to other antibiotics. Levels of resistance to these non-β-lactam antibiotics ranged from 93.2% for tetracycline to 20.5% for ciprofloxacin.

The major sources of MRSA and MSSA (methicillin-sensitive *S. aureus*) strains are shown in Table 3. Among 44 strains of MRSA, 24 (54.5%) were isolated from wounds, 8 (18.2%) from urine, 5 (11.4%) from lower respiratory tract specimens, 4 (9.1%) from boils and abscesses, and 3 (6.8%) from bloodstream infections.

DISCUSSION

The first documented case of MRSA at this hospital was identified in 1995, and the overall rate for the country was about 2% (13,14). The prevalence of MRSA in this study was found to be 9.8%, with a concomitant increase in the percentage of isolates resistant to tetracyclines, gentamicin, co-trimoxazole and erythromycin, though all strains appear to have maintained full susceptibility to vancomycin. In this study, the zone sizes for vancomycin were 15-20 mm in diameter, though the disc diffusion method of susceptibility testing has been reported to be misleading for detecting intermediate or even resistant strains (12). This increase in the rate of resistance to antibiotics, in particular to methicillin, has become a worldwide problem.

The incidence of MRSA strains is particular high in Europe, Asia, and other parts of the world. In Japan, the rate was 60% nationwide and as high as 90% in individual hospitals (15). In Denmark it was found to be 46% (16); it was 46-67.5% in Greek hospitals (17); and in Turkey, 25-80% (18). In North America (19,20) and the Middle East (21), rates of 20-50% and 3-18% have been reported, respectively. MRSA rates from the Caribbean are scanty but one report from Jamaica showed rates of isolation to be 1-2% (22). These different rates among MRSAs from different countries may be attributable to variations in patient populations, the biological characteristics of the *S. aureus* strains, and/or infection control practices (23).

The rate of methicillin resistance among *S. aureus* strains was low in the community (4.1%) compared to that in the hospital (12.5%), but significantly higher than the 1995 rate of 0% in the community ($X^2 = 5.39$; $P < 0.05$). This increase of 4.1% is certainly a cause for concern in Trinidad and may very well represent a trend in the changing epidemiology of MRSA in the late 1990s. Many factors may be at play in the unexpected prevalence of community-acquired MRSA. One reason for this increase may be lateral dissemination from the hospital to the community, most patients diagnosed with MRSA discontinue therapy, once discharged, because of the cost of prescriptions at local pharmacies.

Two reports from Australia suggest that, after patient discharge from hospital, MRSA carriage continues, and that long-term carriers can ultimately become reservoirs for the organisms in the community. Infected superficial wounds and pyodermas are commonly seen in health centers and the offices of general practitioners (unpublished data). Other factors previously identified as contributory to community MRSA include overcrowding (24) and skin sepsis (25). Another factor may be inappropriate prophylactic and therapeutic use of antimicrobials in both hospital and community practices. An earlier report from this country identified over-the-counter sale of antibiotics, without a prescription, as a contributing

factor in the emergence of multi-resistant organisms in the community (26). The six MRSA strains from the community included one each from two diabetic patients, and one isolate each from patients with long standing hypertension, skin sepsis, chronic alcoholism and renal dialysis.

The emergence of MRSA in our hospitals re-emphasizes the need for intensive surveillance and prevalence-culturing of patients and health care providers (HCP) in order to identify all infected and colonized persons. This would require the establishment of MRSA isolation units to physically separate the infected patients and their HCPs from the uninfected ones; treatment protocols for eradicating MRSA from patient and HCP carriers; stringent environmental disinfection in areas housing infected patients; and the application of barrier isolation precautions, including strictly enforced hand washing, to interrupt spread patterns. A previous report from this institution revealed that hand washing practices and sanitation techniques of HCPs at all levels of service were not strictly adhered to (27).

This study has shown that MRSA is not only a problem of hospitalized patients, but also a problem of people within the community. To address this expanding reservoir of multi-resistant organisms, infection control initiatives that involve and include the health centers and general practitioners' offices should be extended to the community in order to monitor and limit the spread of MRSA.

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