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Background. Reports have suggested that the epidemiological profile of invasive Staphylococcus aureus infections is changing. We sought to describe the epidemiological profile of S. aureus bacteremia and to assess whether the incidence and severity of and the antimicrobial resistance rates associated with this bacteremia are increasing.

Methods. Population-based surveillance for S. aureus bacteremias was conducted in the Calgary Health Region (population, 1.2 million) during 2000–2006.

Results. The annual incidence of S. aureus bacteremia was 19.7 cases/100,000 population. Although rates of health care–associated and nosocomial methicillin-susceptible S. aureus (MSSA) bacteremia were similar throughout the study, rates of community-acquired MSSA bacteremia gradually decreased, and rates of methicillin-resistant S. aureus (MRSA) bacteremia dramatically increased. The clonal type predominantly isolated was CMRSA-2 (i.e., Canadian [C] MRSA-2), but CMRSA-10 (USA300) strains have been increasingly isolated, especially from community-onset infections, since 2004. Dialysis dependence, organ transplantation, HIV infection, cancer, and diabetes were the most important risk factors and were comparable for MSSA and MRSA bacteremias. The overall case-fatality rate was higher among individuals with MRSA (39%) than among those with MSSA (24%; P < .0001). The annual overall population mortality rate associated with S. aureus bacteremia did not significantly change during the study.

Conclusions. Although the overall influence of S. aureus bacteremia has not significantly changed, MRSA has emerged as an important etiology in our region.

Staphylococcus aureus is the major cause of bloodstream infection and is associated with significant morbidity and mortality [1–3]. We previously conducted population-based surveillance for all invasive S. aureus infections occurring in the Calgary Health Region (CHR) during 1999–2000 [4]. An overall incidence of 28.4 cases/100,000 population was observed (17.9 cases/100,000 population, for bacteremia), and isolation of methicillin-resistant S. aureus (MRSA) was notably uncommon. Many geographical regions worldwide have reported a recent dramatic increase in the number and severity of infections due to community-associated MRSA [5–13]. This increase in community-associated MRSA infection may be occurring in geographical areas where there is a stable or increasing background rate of methicillin-susceptible S. aureus (MSSA) disease, further increasing the overall influence of S. aureus in recent years [14–16].

To quantify trends in the occurrence, clinical characteristics, and outcome of an infectious disease, population-based studies are optimal. In the design of these studies, all new cases of disease occurring in a defined geographical region are ascertained, and selection bias is minimized; in addition, if the population at risk is known, then incidence rates may be calculated [17, 18]. Few population-based studies investigating the epidemiological profile of invasive or bacteremic S. aureus infections have been conducted, particularly within the current decade [9, 19–26]. The objective of the present study was to conduct population-based surveillance in a large Canadian health region during 2000–2006, to define the epidemiological profile of S. aureus bacteremia and to assess whether the incidence
and severity of bacteremia and the rate of antimicrobial resistance are increasing.

SUBJECTS AND METHODS

Study population. The CHR administers virtually all medical and surgical care to the residents of the cities of Calgary and Airdrie and a large surrounding area (population, 1.2 million) in the province of Alberta, Canada. A detailed description of the CHR is available on the regional Web site [27]. Only patients requiring acute liver, heart, or lung transplantation are routinely referred elsewhere for care. All persons who resided in the CHR and who developed bacteremic S. aureus infection between 1 January 2000 and 31 December 2006 were included in the study. The present study was approved by the Conjoint Health Research Ethics Board at the University of Calgary (Calgary, Alberta, Canada).

Study protocol. An active, population-based surveillance cohort design was used. Surveillance for bacteremic S. aureus infections was conducted by Calgary Laboratory Services, a regional laboratory system that receives >95% of all blood samples submitted for culture from hospitals, nursing homes, and clinics in the CHR. Additional clinical data and details regarding outcomes were obtained for all patients admitted to any of the 4 major acute-care hospitals (representing >95% of CHR admissions), by use of data available from the regional corporate data warehouse.

Definitions. Bacteremic infection with S. aureus was defined by the isolation of that organism from >1 sets of blood culture bottles collected by trained phlebotomists or registered nurses by use of a standardized sterile technique. All S. aureus isolates cultured from blood were deemed to be clinically significant. Clinical isolates were isolated, confirmed to be S. aureus, and tested for antimicrobial susceptibility, by use of standard techniques, according to Clinical and Laboratory Standards Institute guidelines. Phenotypic MRSA strains were confirmed to be mecA positive by means of polymerase chain reaction assay. Typing of MRSA strains was performed at Calgary Laboratory Services during 2000–2004 and at the Provincial Laboratory for Public Health of Southern Alberta during 2005–2006, by use of pulsed-field gel electrophoresis, as described elsewhere [28].

Residency status was established using the 2003 boundaries of the CHR [27]. Incident cases were defined as new, first isolations of MSSA or MRSA; repeated isolation of the same organism (MSSA or MRSA) within 365 days after the first isolation was deemed to represent the same incident infection. Nosocomial bacteremias were those for which the first positive culture result was obtained >48 h after hospital admission or <48 h after discharge. Community-onset infections were those for which the first positive culture result was obtained <48 h after admission or >48 h after discharge from the hospital. These infections were further classified as health care–associated and community-acquired infections, by use of a modification of the definitions set forth by Friedman et al. [29]. Health care–associated community-onset S. aureus bacteremia was also identified based on the presence of ≥1 of the following criteria: (1) discharge of the subject from the adult Home Parenteral Therapy (HPTP) Clinic 2–30 days before bloodstream infection occurred [30]; (2) attendance at a specialized hospital clinic or emergency department 2–30 days before the bloodstream infection occurred; (3) admittance to the CHR acute care hospital for ≥2 days during the 90 days before bloodstream infection occurred; (4) submission of a sample from a patient resident in a nursing home or long-term care facility; or (5) requirement of outpatient hemodialysis. Data on HPTP Clinic assessment and dialysis was not available for children. For these and the other, rare cases of community-onset S. aureus bacteremia for which data were unavailable, they were assumed to be absent. Community-acquired infections were those community-onset bacteremias that were not health care associated. For each patient, a primary diagnosis of the source of S. aureus infection was made using discharge codes and S. aureus culture results obtained during the 48 h before or after the blood culture draw for the index incident and was categorized as described elsewhere [4].

Statistical analysis. Analysis was performed using Stata software (version 9.0; Stata Corporation). Nonnormally distributed variables were reported as median values with interquartile ranges (IQRs) and were compared using the rank-sum test for pairs or the median test for multiple groups. Differences in proportions among categorical data were assessed using Fisher’s exact test, for pairwise comparisons, and the χ² test, for multiple groups. The incidence of bacteremic S. aureus infection was calculated by dividing the number of incident cases by the regional population [31]. For incidence calculations, MRSA bacteremia and MSSA bacteremia were considered independently. Risk factors for the development of S. aureus bacteremia were quantified as described elsewhere [4]. The population at risk was ascertainment or estimated by use of local patient registry data (on HIV infection, dialysis, and transplantation) [32–34], regional or Canadian survey data (on alcoholism, cancer, and other medical comorbid illnesses) [27, 35], or data from published North American epidemiological studies (of inflammatory bowel disease, rheumatoid arthritis, and systemic lupus erythematosus) [36–38]. Risks were expressed as incidence rate ratios (RRs) and were reported with 95% confidence intervals (CIs). Case-fatality and mortality rates were calculated using the number of hospital deaths due to all causes. For all statistical comparisons, P < .05 was deemed to denote statistical significance.

RESULTS

During the 7-year study, 1508 CHR residents had ≥1 incident bacteremic S. aureus infection; 31 patients had 2 incident episodes, and 3 patients had 3 such episodes. Basic demographic
characteristics (age, sex, and residency) and microbiologic data were available for all patients, and additional clinical and outcome information was available for the 1440 (93%) of 1542 incident cases managed at 1 of the 4 major acute-care centers in the CHR. Of the 1542 incident bacteremic S. aureus infections, 599 (39%) were classified as nosocomial cases, 561 (36%) as health care–associated community-onset cases, and 382 (25%) as community-acquired cases. Of 1373 MSSA and 169 MRSA infections, 519 (38%) and 80 (47%) were nosocomial, 491 (36%) and 70 (41%) were health care–associated infections, and 363 (26%) and 19 (11%) were community acquired, respectively. Of the total 561 patients with health care–associated cases, 338 (60%) had been recently managed in an emergency department or specialized hospital clinic, 287 (51%) had recently been hospitalized, 169 (30%) were receiving dialysis, and 72 (13%) were residents of nursing homes or long-term care facilities.

Incidence. The overall annual incidence of S. aureus bacteremia was 19.7 cases/100,000 population, and, for bacteremia due to MSSA or MRSA, the overall annual incidences were 17.5 and 2.2 cases/100,000 population/year, respectively. Although no statistically significant difference in the overall annual rates of S. aureus bacteremia was observed (P = .74), a slightly decreasing overall annual incidence rate was noted during the first 5 years of the study, with an increase occurring again in the last 2 years of the study (figure 1). Although rates of both health care–associated community-onset and nosocomial MSSA bacteremia were not significantly different throughout the duration of the study, rates of community-acquired MSSA bacteremia gradually decreased (P = .01) (figure 2). On the other hand, rates of MRSA bacteremia dramatically increased (P < .001). This finding was principally attributable to major increases in nosocomial (P = .001) and health care–associated community-onset disease (P < .001) (figure 3).

Risk factors. The incidence of both MSSA and MRSA bacteremia increased with advancing age (figure 4). The median patient age was 62.8 years (IQR, 46.3–76.2 years) and was significantly (P < .001) lower for patients with community-acquired infections (54.9 years; IQR, 34.5–71.5 years) than for patients with nosocomial infections (67.1 years; IQR, 50.7–77.3 years) and health care–associated infections (64.2 years; IQR, 48.1–77.8 years). Overall, 957 (62%) of 1542 incident episodes occurred in males (RR, 1.64; 95% CI, 1.48–1.82; P < .0001), and this proportion did not vary significantly yearly during the study (P = .70). For males, the risk for MSSA-associated bacteremia was 1.68-fold higher (95% CI, 1.50-fold to 1.88-fold; P < .0001) than that for females, and this excess risk was observed in each year of the study. Although an overall excess risk of MRSA bacteremia was also observed for males (RR 1.39; 95% CI, 1.01–1.91; P = .04), this excess risk was only significantly observed in a single year (2005) (RR, 2.66; 95% CI, 1.40–5.32; P = .001).

Most of the inpatients (1102 [77%] of 1440) had significant chronic comorbid illnesses and/or alcoholism, and this finding was noted significantly more frequently for nosocomial (487 [81%] of 598) infections and health care–associated (392 [80%] of 488) infections than for those with community-acquired (223 [63%] of 354) infections (P < .0001). A number of selected conditions were assessed as risk factors for acquisition of S. aureus bacteremia, and these conditions are shown in table 1. Dialysis dependence, organ transplantation, HIV infection, cancer, and diabetes were the most important risk factors, and the risks of acquiring MSSA and MRSA bacteremia were similar (table 1). Of the 276 patients with cancer, 151 (55%) had malignant solid tumors, 69 (25%) had hematologic malignancies, 2 (1%) had both solid tumors and hematologic malignancies, and 54 (20%) patients had a history of neoplasm disease. Nineteen infections occurred among organ transplant recipients, including 8 kidney, 3 heart, and 3 liver recipients and 1 kidney/liver recipient, and the transplanted organ was unspecified for 4 cases. No significant trend in the occurrence of comorbid illnesses was evident during the 7 years of the study.
Clinical characteristics and outcome. Primary bacteremia was the most common clinical syndrome observed, with bone and joint, soft tissue, and lower respiratory tract infections being the most common focal sources of bacteremia (table 2). Although MRSA was the cause of 163 (11%) of 1440 of the incident infections, a significantly (P < .0001) higher proportion of intra-abdominal/pelvic and respiratory sources was due to MRSA (table 2). Of 220 lower respiratory infections, 20 (9%, with 5 of the infections due to MRSA) were empyemias, and 5 (3%, with none of the infections due to MRSA) were necrotizing. A total of 34 (15%) of 227 bone and joint infections involved vertebral osteomyelitis/discitis. Of 86 endovascular cases, 79 (92%) were due to endocarditis, with the remainder due to septic thrombophlebitis. Of the 12 CNS infections, 11 were meningitis and 1 was a subdural empyema/subdural abscess. Although the distribution of sites of focal infection varied from year to year, no clear trend was observed over the study period.

The overall median length of hospitalization was 16.9 days (IQR, 8.1–40.2 days) and was significantly (P < .0001) longer for individuals with nosocomial infections (32.1 days; IQR, 15.9–63.6 days) than for individuals with health care–associated (11.0 days; IQR, 5.8–23.7 days) and community-acquired (11.6 days; IQR, 6.2–24.5 days) infections. The median time from admission to development of nosocomial bacteremia was 9.7 days (IQR, 4.6–20.0 days) and was longer for individuals with MRSA bacteremia than for individuals with MSSA bacteremia (13.5 days [IQR, 7.1–34.8 days] vs. 9.4 days [IQR, 4.3–18.6 days]; P = .0001). The case-fatality rate was 25% (366 deaths among 1440 patients) and was highest for patients with nosocomial infections (35%; 207 deaths among 598 patients), followed by those with health care–associated infections (21%; 104 deaths among 488 patients; P < .0001) and community-acquired infections (16%; 55 deaths among 354 patients; P = .04, vs. health care–associated infections). The case-fatality rate for patients with MRSA bacteremia was significantly higher than that for patients with MSSA bacteremia (39% [64 deaths among 163 patients] vs. 24% [302 deaths among 1277 patients]; P < .0001). Although the population mortality rate associated with MRSA
bacteremia was increasing during the study, no significant overall increase in the rate of death due to *S. aureus* bacteremia was observed (figure 5).

**MICROBIOLOGICAL PROFILE**

Results of susceptibility testing were available for analysis of 1496 incident infections (97%). Overall ciprofloxacin resistance (223 [15%] of 1483 infections) increased significantly during the study period. However, this increase was solely attributable to an increase, in the later years of the study, in the number of MRSA strains with a high but stable rate of ciprofloxacin resistance (150 [90%] of 167 strains). Both MSSA (23 [2%] of 1327 strains) and MRSA (6 [4%] of 167 strains) were associated with low rates of resistance to trimethoprim-sulfamethoxazole, and these rates did not significantly change during the course of the study. Only 2 of 1483 isolates were resistant to rifampin, 1 of 1491 isolates had reduced susceptibility to vancomycin, and none of the 174

<table>
<thead>
<tr>
<th>Condition</th>
<th>Age group</th>
<th>RR (95% CI), by bacteremia type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodialysis</td>
<td>20+</td>
<td>360.2 (308.5–418.8) 364.4 (309.0–427.7) 330.8 (203.0–516.6)</td>
</tr>
<tr>
<td>Cancer</td>
<td>20+</td>
<td>13.6 (11.8–15.6) 13.9 (12.0–16.1) 11.4 (7.3–17.2)</td>
</tr>
<tr>
<td>HIV infection</td>
<td>All</td>
<td>17.1 (9.9–27.4) 17.0 (9.5–28.1) 17.8 (2.1–65.5)</td>
</tr>
<tr>
<td>Organ transplant</td>
<td>20+</td>
<td>16.0 (9.3–25.8) 14.9 (8.1–25.1) 25.4 (5.2–75.5)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>12+</td>
<td>10.6 (9.3–11.9) 10.0 (8.8–11.5) 14.7 (10.4–20.6)</td>
</tr>
<tr>
<td>Heart disease</td>
<td>12+</td>
<td>6.9 (6.0–7.8) 6.7 (5.8–7.7) 8.1 (5.6–11.7)</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>All</td>
<td>5.0 (3.8–6.4) 4.6 (3.4–4.6) 8.0 (3.9–14.8)</td>
</tr>
<tr>
<td>COPD</td>
<td>12+</td>
<td>3.8 (3.2–4.5) 3.4 (2.8–4.1) 7.3 (4.8–11.0)</td>
</tr>
<tr>
<td>Stroke</td>
<td>12+</td>
<td>3.4 (2.5–4.6) 2.9 (2.0–4.1) 7.2 (3.5–13.3)</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>20+</td>
<td>2.7 (2.2–3.2) 2.7 (2.2–3.3) 2.5 (1.3–4.2)</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>20+</td>
<td>2.6 (1.8–3.7) 2.7 (1.8–3.9) 1.9 (0.4–5.6)</td>
</tr>
<tr>
<td>SLE</td>
<td>20+</td>
<td>1.8 (0.8–3.5) 2.1 (1.0–4.0) . . .</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>All</td>
<td>1.5 (0.4–3.9) 1.7 (0.5–4.4) . . .</td>
</tr>
<tr>
<td>Crohn disease</td>
<td>All</td>
<td>1.2 (0.4–2.9) 1.4 (0.4–3.2)</td>
</tr>
<tr>
<td>Asthma</td>
<td>12+</td>
<td>0.3 (0.2–0.5) 0.4 (0.2–0.5) 0.2 (0–0.6)</td>
</tr>
</tbody>
</table>

**NOTE.** CI, confidence interval; COPD, chronic obstructive pulmonary disease; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *S. aureus*; RR, rate ratio; SLE, systemic lupus erythematosus.

Table 2. Primary diagnoses of 1440 bacteremic *Staphylococcus aureus* infections.

<table>
<thead>
<tr>
<th>Primary diagnosis</th>
<th>All (n = 1440)</th>
<th>MRSA associated</th>
<th>Nosocomially acquired</th>
<th>Health care associated</th>
<th>Community acquired</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary bacteremia</td>
<td>586 (41)</td>
<td>61 (10)</td>
<td>332 (67)</td>
<td>183 (31)</td>
<td>71 (12)</td>
</tr>
<tr>
<td>Infection, by site</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone and joint</td>
<td>227 (16)</td>
<td>15 (7)</td>
<td>38 (17)</td>
<td>82 (36)</td>
<td>107 (47)</td>
</tr>
<tr>
<td>Soft tissue</td>
<td>224 (16)</td>
<td>23 (10)</td>
<td>87 (39)</td>
<td>84 (38)</td>
<td>53 (24)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>220 (15)</td>
<td>36 (16)</td>
<td>102 (46)</td>
<td>71 (32)</td>
<td>47 (21)</td>
</tr>
<tr>
<td>Endovascular</td>
<td>86 (6)</td>
<td>7 (8)</td>
<td>13 (15)</td>
<td>28 (33)</td>
<td>45 (52)</td>
</tr>
<tr>
<td>IA/pelvic</td>
<td>79 (5)</td>
<td>20 (25)</td>
<td>18 (23)</td>
<td>36 (46)</td>
<td>25 (32)</td>
</tr>
<tr>
<td>CNS</td>
<td>12 (1)</td>
<td>1 (8)</td>
<td>4 (33)</td>
<td>3 (25)</td>
<td>5 (42)</td>
</tr>
<tr>
<td>Other</td>
<td>6 (6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NOTE.** Data are no. (%) of infections. CNS, central nervous system; IA, intra-abdominal; MRSA, methicillin-resistant *S. aureus*.

a All ages are expressed in years.
isolates tested against linezolid demonstrated reduced susceptibility. Pulsed-field gel electrophoresis typing was available for 145 cases (86% of the total 169 MRSA infections). The majority of infections (104 cases [72%]) were CMRSA-2; 27 (19%), CMRSA-10; 4 (3%), CMRSA-6; 4 (3%), CMRSA-8; 3 (2%), CMRSA-1; 2 (1%), CMRSA-7; and 1 (1%), CMRSA-4. Although CMRSA-2 was predominant from the outset, it was typically associated with nosocomial (55 [53%]) and health care–associated (42 [40%]) infections, and community acquisition (7 [7%]) was uncommon. In contrast, the predominance of CMRSA-10 caused community-onset infections (8 were community-acquired [1 in 2004, 5 in 2005, and 2 in 2006]; 12, health care associated [7 in 2005 and 5 in 2006]; and 7, nosocomial [5 in 2005 and 2 in 2006]), and infections first appearing in 2004 caused nearly one-third (26 [30%] of 88) of all subsequent MRSA bloodstream infections.

DISCUSSION

In the present article, we reported contemporary population-based data describing the incidence of, risk factors for, and outcome of S. aureus bacteremia in a large Canadian population (∼8 million person-years of observation). We also present novel detailed data on the emergence of MRSA bacteremia in a population with a concomitant assessment of MSSA bacteremias, allowing for an evaluation of the overall influence on the population.

Few contemporary studies are available for comparison of our incidence rate of 19.7 cases/100,000 population/year. Benfield et al. [21] and Frederiksen et al. [20] reported annual incidence rates of 30.5 and 8.4 cases/100,000 population among adults and children in Denmark during 1996–2000, respectively, for an overall calculated incidence rate of ∼24.4 cases/100,000 population/year. Morgan et al. [25] noted an incidence rate of 18 cases/100,000 population, for isolation of S. aureus from blood and/or CSF in Wales in 1996. Griffiths et al. [16], in a subsequent report from England and Wales covering 1993–2002, identified a rate of ∼20 cases/100,000 population/year in the latter years of their study. Morin and Hadler [39] investigated community-onset bacteremia in 4 metropolitan regions in Connecticut in 1998, and they found a rate of 17 cases/100,000 population. This rate is much higher than our incidence rate of 12.1 cases/100,000 population for health care–associated and community-acquired S. aureus bacteremia combined. Lyytikainen et al. [23] performed surveillance in Finland during 1995–2001. They found a lower overall rate of 14 cases/100,000 population, but this rate increased during the study, with 17 cases/100,000 population noted in 2001 [23]. McDonald et al. [26] reported S. aureus bacteremia on the island of Ireland in 1999, as well as incidence rates of 20.4 cases/100,000 population in Northern Ireland and 24.5 cases/100,000 population in the Republic of Ireland. Most recently, Jacobssen et al. [19] performed surveillance for invasive S. aureus infections in western Sweden during 2003–2005 and found an overall rate of 31.4 cases/100,000 population, of which 83% of cases (i.e., 26 cases/100,000 population) were bacteremic. Kleven et al. [9] found an age-, sex-, and race-standardized incidence of invasive MRSA infection of 31.8 cases (∼24 cases, for bacteremia) per 100,000 population in the United States in 2005, a rate >10-fold higher than what we observed.

Our present study is important in that we document the emergence of MRSA at the population level that allows concomitant assessment of the burden of MSSA infection. Before we conducted this study, the clinical impression in our region was that S. aureus bacteremias were increasing at an alarming rate. Although we found this to be true for MRSA bacteremia, this was not the case for MSSA bacteremia. Numerous studies have noted

Figure 5. Mortality rate (no. of deaths per 100,000 population) associated with Staphylococcus aureus bacteremia, Calgary Health Region, 2000–2006. MRSA, methicillin-resistant S. aureus; MSSA, methicillin-susceptible S. aureus.
a recent increase in the occurrence and severity of MRSA infections, particularly in relation to community-associated strains [8, 9, 40]. In addition, several population-based studies indicated that the incidence of *S. aureus* bacteremia increased during the previous decades [20, 21, 23]. However, there is less known about how the recent emergence of MRSA has influenced the overall impact of *S. aureus* disease in populations. Data from passive surveillance in England and Wales during 1993–2002 demonstrated that, although the number of MSSA bacteremias was relatively constant, the number of MRSA bacteremias increased significantly, resulting in an overall population influence due to *S. aureus* bacteremia [16]. In contrast, we observed a decrease in the incidence of MSSA infection in association with an increase in the incidence of MRSA infection (figure 1). It is of note that, in the last 2 years of our study, there may be a trend developing toward an increase in the overall burden of *S. aureus* infections. Only further population-based surveillance in our region and elsewhere will provide a definitive answer as to whether the overall burden of invasive/bacteremic *S. aureus* infections is increasing in association with the emergence of MRSA.

There are a number of important observations regarding the epidemiological profile of MRSA bacteremia in our region. Although MRSA infections were rare before and early on in our study, they were responsible for 1 in 5 incident *S. aureus* bacteremias in 2005–2006. This finding has important implications for empirical antimicrobial therapy for patients with suspected *S. aureus* infections. In recent years, in the strains and patients affected, there has also been a major shift from predominantly nosocomially acquired CMRSA-2 infections to an increasing proportion of community-onset (health care-associated and community-acquired) CMRSA-10 infections.

Our current data support our previous observations and those of others with respect to risk factors for acquisition of invasive/bacteremic *S. aureus* infections. Population-based studies have consistently identified that males and very young and elderly individuals are at increased risk for such infections [4, 9, 19, 20, 23, 39]. However, although several studies have noted a high frequency of chronic comorbid illnesses among patients with *S. aureus* bacteremia, only 2 previous studies have quantified the actual magnitudes of risks. The first study is our previous study investigating invasive *S. aureus* infections in Calgary in 1999–2000, and the other study is the more recently conducted study performed by Jacobsson and colleagues in the catchment area of Skaraborg Hospital in western Sweden during 2003–2005 [4, 19]. These studies both demonstrated that, by far, the most important risk factor is a requirement for dialysis, with a number of other illnesses, including diabetes and cancer, also increasing the risk. Although our current study differs from these studies in that it includes only bacteremic cases, the risk factors identified, as well as their magnitude, are similar to those associated with all invasive cases (table 1). Our present study adds 2 main novel observations. First, the distribution and magnitude of comorbidity risk factors for acquiring MRSA and MSSA are comparable (table 1). Second, we identified that hepatitis C is associated with a 5-fold increased risk for *S. aureus* bacteremia. It remains unknown whether this increased risk is attributable to cirrhosis, active viral hepatitis, or ongoing illicit drug use or whether it is related to adverse effects of treatment [41].

There are some limitations to our risk factor analysis that merit discussion. Because of a lack of both numerators and denominators for use in calculations, we were unable to evaluate a number of specific risk factors for acquisition of MRSA, including illicit injection drug use, socioeconomic disadvantage, and incarceration [8, 40]. In addition, the risk factors that we identified are based on a pooled analysis of community- and hospital-onset cases, and these may have different magnitude within different acquisition groups. Finally, because, in some cases, we used estimates for prevalence data based on survey data obtained in other North American populations, the exact magnitude of our reported relative risks should be interpreted cautiously, especially when they are close to unity.

There are few population-based studies with which to compare our study in terms of mortality outcomes, because many either have not reported death outcomes of hospital-onset cases. Most studies have not reported death outcomes or have used methods that preclude direct comparison [16, 19, 25, 26]. Our observation of an overall case-fatality rate of 25% for *S. aureus* bacteremia compares with the rate of ~21% noted in Denmark during 1996–2000 [20, 21] and with 28-day and 90-day case-fatality rates of 17% and 24%, respectively, noted in Finland during 1995–2001 [23]. The case-fatality rate of 11% reported by Morin and Hadler [39] for community-onset cases is considerably lower than the rate of 19% that we reported for community-onset cases. However, because Morin and Hadler [39] incorporated population denominator data, mortality rates are better than case-fatality rates for comparison among different regions. Our mortality rate of 4.7 deaths/100,000 population/year (2.0 deaths/100,000 population/year, for community-onset disease) is very similar to the overall mortality rate most recently reported from Denmark (5.1 deaths/100,000 population/year) [20, 21], Finland (4.2 deaths/100,000 population/year) [23], and the United States (1.9 deaths/100,000 population/year) [39]. It is notable that both the studies from Denmark and that from Finland reported changing mortality rates, whereas the rates that we noted remained stable over the duration of the study. Kleven et al. [9] recently reported in-hospital case-fatality and standardized mortality rates of 18% (of cases) and 6.3 deaths/100,000 population, respectively, for invasive MRSA infection in the United States, with the former rate much lower and the latter rate much higher than the rates that we observed.

In summary, the incidence of, risk factors for, and outcomes associated with *S. aureus* bacteremia have not significantly changed in our region during 2000–2006. However, MRSA has emerged as an important cause of bloodstream infection.
References


