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Population-based laboratory assessment of the burden of community-onset bloodstream infection in Victoria, Canada

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SUMMARY

Although community-onset bloodstream infection (BSI) is recognized as a major cause of morbidity and mortality, its epidemiology has not been well defined in non-selected populations. We conducted population-based laboratory surveillance in the Victoria area, Canada during 1998–2005 in order to determine the burden associated with community-onset BSI. A total of 2785 episodes were identified for an overall annual incidence of 101·2/100 000. Males and the very young and the elderly were at highest risk. Overall 1980 (71%) episodes resulted in hospital admission for a median length of stay of 8 days; the total days of acute hospitalization associated with community-onset BSI was 28 442 days or 1034 days/100 000 population per year. The in-hospital case-fatality rate was 13%. Community-onset BSI is associated with a major burden of illness. These data support ongoing and future preventative and research efforts aimed at reducing the major impact of these infections.

Key words: Bloodstream infections, epidemiology.

INTRODUCTION

Bloodstream infections (BSI) are a major cause of morbidity and mortality [1–6]. In contrast with nosocomial BSI where an extensive body of literature exists, less is known about the epidemiology of community-onset BSI [1, 3, 4, 7, 8]. While several large series describing the occurrence and outcomes of community-onset BSI have been reported, they typically have been hospital-based series for which the population at risk is unknown and therefore the burden of disease not quantifiable [1, 2, 9, 10]. Furthermore, although numerous population-based studies assessing community-onset BSI have been reported, these studies to date have largely been restricted to the assessment of specific aetiologies or selected patient subgroups [11–13]. As a result, the overall occurrence and outcome associated with community-onset BSI remains poorly defined [3, 5].

Defining the burden of community-onset BSI is required to place its relative importance among other health conditions for setting healthcare service and research funding priorities. We therefore conducted population-based laboratory surveillance in the Victoria area of Canada in order to define the overall and species-specific incidence of, and the associated

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hospital-related morbidity and mortality associated with community-onset BSI.

METHODS

Study population

The Vancouver Island Health Authority (VIHA) is one of five health regions within the province of British Columbia, Canada. It administers virtually all publicly funded healthcare to the >750 000 residents of Vancouver Island and an adjacent area of the mainland. The south local health area (SLHA) of VIHA (2005 population 357 768) includes the Greater Victoria area and the surrounding communities of Saanich, Sooke, and the Gulf Islands. The SLHA has three main acute-care institutions, with a total of 854 acute-care beds. These institutions provide nearly all of the acute inpatient care for residents of the SLHA with only patients requiring acute bone marrow or organ transplantation and a few other highly specialized services routinely referred to Vancouver. All residents of the SLHA with identified community-onset BSI during the 8-year period between 1 January 1998 and 31 December 2005 were included in the study. Patients were defined as SLHA residents based on postal codes. Those patients without a listed postal code who had a British Columbia healthcare number were also included as area residents.

Population-based surveillance

An active, population-based, laboratory surveillance design was utilized. All BSI occurring in SLHA residents were identified through the regional hospital laboratories. These hospital laboratories perform all microbiology testing on all samples submitted from hospitals and emergency departments and a large proportion from the community. There is one private laboratory in the region that provides microbiology services in the community setting but positive blood cultures are uncommon and estimated to represent <1% of all positive blood cultures in the SLHA population. Basic demographic, hospital length of stay, and in-hospital mortality outcome information was obtained from the regional microbiology database.

Laboratory procedures and definitions

All blood was cultured using the BACTEC 9240 automated instrument (Becton Dickinson, USA). A blood culture set consisted of an aerobic/anaerobic lytic bottle pair of BACTEC bottles obtained from a single draw. Standard practice during this study period was to draw sets of blood cultures from two different sites. Organisms were isolated and speciated using standard methods. A BSI was defined as the growth of a pathogenic organism from at least one set of blood cultures. Organisms frequently associated with contamination including coagulase-negative staphylococci, viridans group streptococci, or *Bacillus*, *Corynebacterium*, or *Propionibacterium* species were *a priori* required to have at least two sets of blood cultures positive to be included in analysis [14]. Repeat infections with the species in a given patient within a 1-year period were classified as a single incident case. Community-onset BSI were classified as those obtained from patients that were not admitted to hospital or identified within the first 2 days of stay in those admitted to an acute-care hospital. Infections occurring in the first 28 days of life were also classified as nosocomial and were excluded. All isolates obtained within a 2-day period were considered to represent the same episode of disease; positive cultures with different species separated by more than 2 days were considered new episodes. Polymicrobial BSI were those that had more than one species co-isolated within a 2-day period of the index culture draw.

Statistical analysis

All analyses were performed using Stata version 11.2 (StataCorp, USA). Differences in proportions among categorical data were assessed using Fisher's exact test. Medians with interquartile range (IQR) were used to describe skewed continuously distributed variables and were compared using the Mann–Whitney test. Incidence rates were calculated using regional demographic data (BC STATS, BC Ministry of Labour and Citizens' Services, Government of British Columbia, Victoria, BC). Age- and gender-specific risks were calculated and reported as risk ratios (RR) with 95% confidence intervals (CI) as described previously [15].

RESULTS

During the 8 years of surveillance, a total of 2785 episodes of community-onset BSI were identified among 2534 SLHA residents for an overall annual incidence of 101·2/100 000 population. One hundred and eighty-nine (7%) patients had second incident

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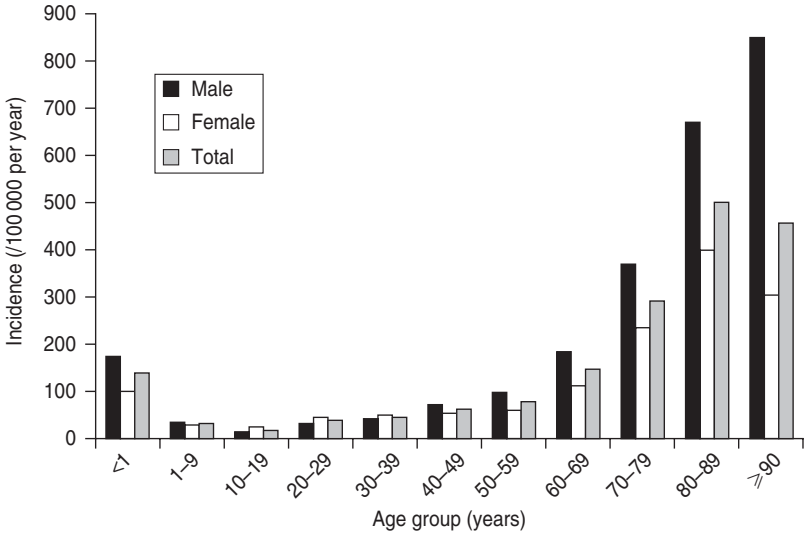

Fig. 1. Age- and gender-specific incidence of community-onset bloodstream infections, South Local Health Area, British Columbia, 1998–2005.

episodes of BSI and 41 (1%) had three, 14 had four, six had five and one patient had six episodes during the course of the study. There was no significant ($P=0{\cdot}14$) year to year variability in the annual incidence.

Demographic risk factors

The median age was 70·1 (IQR, 47·9–80·7) years and 1493 (54%) episodes occurred in males. A relationship was observed between age and gender and the incidence of community-onset BSI with the very young and the elderly at highest risk as shown in Figure 1. The overall incidence of community-onset BSI was higher in males than in females (112·8 *vs.* 90·53/100 000; RR 1·25, 95% CI, 1·15–1·34, $P<0{\cdot}0001$) and this was predominantly related to an increased risk in males aged ⩾60 years (358·4 *vs.* 232·3/100 000; RR, 1·54, 95% CI, 1·40–1·70, $P<0{\cdot}0001$).

Microbiology

Although a wide range of organisms caused community-onset BSI, the three species *Escherichia coli*, *Staphylococcus aureus*, and *Streptococcus* (*Str.*) *pneumoniae* were responsible for more than one-half of all cases as shown in Table 1. Among the ten most common organisms causing community-onset BSI, males were at increased risk with the notable exception of *E. coli* that was more common in females (Table 1). Overall, 264 (9%) of episodes of community-onset BSI were of polymicrobial aetiology, and this varied by species (Table 1). Compared to monomicrobial BSIs, polymicrobial infections were associated with older median patient age (73·3 *vs.* 69·8 years, $P=0{\cdot}003$). Of 831 *E. coli* BSI, six (1%) were due to extended-spectrum β-lactamase-producing strains and in 405 *S. aureus* cases, 32 (8%) were methicillin-resistant.

Acute-care hospital admission and outcome

Overall 1980 (71%) episodes resulted in admission to one of the three regional acute-care institutions, representing 0·88% of all admissions during 1998–2005 to these institutions. Admitted patients were less likely to be male (957/1980; 52% *vs.* 335/805, 58%, $P=0{\cdot}001$) and had higher median age (71·1 *vs.* 66·8, $P=0006$) compared to patients who were not admitted. The hospital length of stay was a median of 8 (IQR 4–16) days; the total days of acute hospitalization associated with community-onset BSI was 28 442 days or 1034 days/100 000 population per year. Of the 1980 episodes of community-onset BSI associated with hospital admission, 250 died for an in-hospital case-fatality rate (CFR) of 12·6%. For patients surviving to hospital discharge, the median length of stay was 8 days (IQR 4–16). Rates of hospital admission, length of stay, and CFR varied by species as shown in Table 2. The CFR associated with polymicrobial infections was 17% (32/191) compared to 12% (218/1, 789) for monomicrobial infections ($P=0{\cdot}085$).

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Table 1. *Comparison of the epidemiological characteristics of the ten most common causes of community-onset bloodstream infections, South Local Health Area, British Columbia, 1998–2005*

Species	*N*	Incidence (/10^5 population per year)			Risk ratio for males (95% CI)	Polymicrobial	Median age (years)
		Total	Male	Female			
Escherichia coli	879	32·0	28·2	35·5	0·79 (0·69–0·91)	101 (11%)	75 (61–82)
Staphylococcus aureus	426	15·5	19·5	11·8	1·66 (1·36–2·03)	35 (8%)	51 (38–75)
Streptococcus pneumoniae	281	10·2	11·0	9·5	1·17 (0·92–1·48)	5 (2%)	55 (33–78)
Klebsiella pneumoniae	157	5·7	7·0	4·6	1·53 (1·10–2·13)	45 (29%)	78 (66–83)
Enterococcus faecalis	100	3·6	5·2	2·2	2·40 (1·55–3·79)	30 (30%)	75 (64–83)
Coagulase-negative staphylococci	92	3·3	4·3	2·5	1·76 (1·13–2·76)	8 (9%)	70 (53–80)
Streptococcus agalactiae	69	2·5	2·9	2·2	1·32 (0·80–2·20)	0	68 (49–79)
Streptococcus pyogenes	62	2·3	2·5	2·0	1·23 (0·72–2·09)	4 (6%)	45 (29–73)
Group G streptococci	60	2·2	3·2	1·3	2·52 (1·42–4·64)	3 (5%)	74 (62–80)
Bacteroides fragilis	57	2·1	2·6	1·5	1·71 (0·98–3·07)	30 (53%)	73 (56–83)
Other	938	34·1	41·8	27·0	1·55 (1·36–1·77)	330 (35%)	71 (51–80)

CI, Confidence interval.

Table 2. *Admission to acute-care hospitals and outcome associated with different aetiologies of community-onset bloodstream infections, South Local Health Area, British Columbia, 1998–2005*

Species	Number admitted	Median stay (IQR), days	In-hospital death
Escherichia coli	604 (69%)	6 (4–11)	61 (10%)
Staphylococcus aureus	321 (75%)	13 (6–28)	54 (17%)
Streptococcus pneumoniae	208 (74%)	6 (3–13)	25 (12%)
Klebsiella pneumoniae	103 (66%)	7 (4–12)	16 (16%)
Enterococcus faecalis	67 (67%)	11 (5–34)	6 (9%)
Coagulase-negative staphylococci	67 (73%)	8 (3–13)	11 (16%)
Streptococcus agalactiae	45 (65%)	6 (5–16)	4 (9%)
Streptococcus pyogenes	40 (65%)	10 (6–18)	2 (5%)
Group G streptococci	45 (75%)	10 (7–22)	6 (13%)
Bacteroides fragilis	47 (82%)	7 (5–15)	12 (26%)
Other	677 (72%)	9 (4–17)	97 (14%)

IQR, Interquartile range.

DISCUSSION

In this study we document the major burden of illness associated with community-onset BSI. We found that community-onset BSI is common with nearly 1/1000 residents per year affected, is associated with a high rate of utilization of hospital care of about 1 day/100 residents per year, and is associated with death in 1/10 people infected. It must be recognized that BSI is only one manifestation of bacterial disease, probably reflecting only the 'tip of the iceberg' of the true burden of community-onset infections and that different foci of infections with bloodstream involvement will have different clinical courses and outcomes.

There are few previous population-based studies with which to compare our results [3–6]. Laupland *et al.* reported population-based surveillance in the Calgary area of Canada during 2000–2004 and found a lower overall incidence of community-onset BSI of 82/100 000 but a similar in-hospital CFR of 13% to the present study [5]. It is important to note that the Calgary study strictly excluded all potential contaminants such as coagulase-negative staphylococci

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whereas in the present study these were included if two or more sets were positive. Furthermore, differences in sociodemographic profiles of the two regions may influence incidence rates. To explore these possibilities, we age- and gender-standardized (<1 year and per decile thereafter) our current study results to the Calgary Health Region 2002 population. The adjusted overall incidence rate was 73·1/100 000. After further excluding all potential contaminants the adjusted rate was 68·9/100 000 population. This observation underscores the importance of utilizing like-definitions and age- and gender-standardization when comparing surveillance results from different populations.

There have been two studies from Denmark that have evaluated the epidemiology of bacteraemia at the population level [3, 4]. Madsen *et al.* conducted population-based surveillance for all causes of bacteraemia in North Jutland County, Denmark from 1981 to 1994 and found 7198 bacteraemias for an overall incidence of 106·2/100 000 and a CFR of 24% [4]. However, they did not separately report rates for community- and hospital-onset cases such that we are not able to directly compare their results to our present study. In another study from North Jutland County, Pedersen *et al.* reported on 1844 patients aged ⩾15 years with community-acquired bacteraemia during 1992–1997 [3]. Although they did not report incidence rates in their study, based on a population estimate of 400 000 this would correspond to an approximate annual incidence of 77/100 000 population aged ⩾15 years [16]. They observed a 30-day CFR of 18% that is substantially higher than that observed in our study. While our data are not directly comparable because they excluded children aged ⩽14 years (who have a low mortality rate due to bacteraemia), notably they found that the CFR decreased from 20% in 1992–1995 to 15% in 1996–1997 such that the more recent data is similar to our observed rate.

Uslan and colleagues reported on 650 BSI occurring in residents of Olmsted County, USA (population 124 277) between 2003 and 2005 [6]. They reported an overall age- and gender-adjusted incidence of 189/100 000 population of which 124 (19%) were nosocomial, 237 (36%) were healthcare associated, and 289 (44%) were community acquired. The incidence of community-onset BSI was therefore 153/100 000, a much higher rate than that seen in our present and previous studies. The overall CFR was 13·5% but was not reported separately for community-onset disease to allow comparison.

It is notable that the three pathogens *E. coli*, *S. aureus*, and *Str. pneumoniae* were responsible for more than one-half of all community-onset bacteraemias. Population-based studies conducted in high-income countries have consistently identified *E. coli* as the most frequent cause of community-onset BSI with rates of 23-28/100 000 observed in Denmark, Canada, and Australia [3, 5, 17, 18], and approximately 38/100 000 in an American study [19]. Rates of community-onset *S. aureus* BSI have demonstrated considerable variability in population-based studies including rates of 13·5/100 000 in Calgary [5], 17 and 29/100 000 in two different American studies [12, 20], 6/100 000 in North Denmark [3], and 19/100 000 in western Sweden [21]. Rates of pneumococcal BSI have been changing significantly in different populations in recent years due to the use of protein polysaccharide pneumococcal vaccine [5, 22–26].

There are some methodological strengths and limitations of this study that merit discussion. First, by including all residents with BSI occurring in the region and excluding non-residents, selection bias was minimized. This is important as it has been recognized that inclusion of patients external to a base population may lead to false attribution of incidence rates and determinants of disease resulting from 'referral bias' [27]. However, it must be recognized that because a positive blood culture is a requisite for diagnosis of a BSI, patients who do not have blood cultures drawn will not be diagnosed with this condition. Similarly, those who are treated with antibiotics prior to blood culture draw will typically have negative blood cultures. These factors will therefore potentially lead to an underestimate of the true rate of disease. A second limitation of this study is that we were not able to classify patients with community-onset disease further into those who had community-acquired disease and those who had healthcare-associated community-onset disease [28]. This is important because infections in this latter category have many characteristics midway between hospital- and community-acquired disease. Furthermore, we did not identify patients who had been recently discharged from hospital who may have had a positive blood culture within 2 days of discharge. This is relevant as these cases are usually classified as nosocomial and in this study they would have been included as community-onset disease. Third, there was a fairly high rate (29%) of non-admission to hospital observed and we do not have

further outcome data on this cohort. Finally, it would have been valuable to have information as to whether patients had severe disease as measured by requirement for admission to an intensive-care unit.

In conclusion, this study documents the major burden of community-onset BSI on a non-selected population. These data support ongoing and future preventative and research efforts aimed at reducing the major impact of these infections.

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DECLARATION OF INTEREST

None.

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