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Burden of community-onset bloodstream infection: a population-based assessment

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SUMMARY

Although community-onset bloodstream infection (BSI) is recognized to be a major cause of morbidity and mortality, there is a paucity of population-based studies defining its overall burden. We conducted population-based laboratory surveillance for all community-onset BSI in the Calgary Health Region during 2000–2004. A total of 4467 episodes of community-onset BSI were identified for an overall annual incidence of 81·6/100 000. The three species, *Escherichia coli*, *Staphylococcus aureus*, and *Streptococcus pneumoniae* were responsible for the majority of community-onset BSI; they occurred at annual rates of 25·8, 13·5, and 10·1/100 000, respectively. Overall 3445/4467 (77%) episodes resulted in hospital admission representing 0·7% of all admissions to major acute care hospitals. The subsequent hospital length of stay was a median of 9 (interquartile range, 5–15) days; the total days of acute hospitalization attributable to community-onset BSI was 51 146 days or 934 days/100 000 annually. Four hundred and sixty patients died in hospital for a case-fatality rate of 13%. Community-onset BSI is common and has a major patient and societal impact. These data support further efforts to reduce the burden of community-onset BSI.

INTRODUCTION

Bloodstream infections are a major cause of morbidity and mortality [1, 2]. In contrast with nosocomial bloodstream infections where an extensive body of literature exists, less is known about the epidemiology of community-onset bloodstream infections (BSI) [1, 3–6]. 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, 7, 8]. Furthermore, although numerous population-based studies that have assessed community-onset BSI have been reported, these studies to date have largely been restricted to the assessment of specific aetiologies or selected patient subgroups [9–11]. To our knowledge, the only population-based assessments of all community-onset BSI occurring in a non-selected population have been reported from Denmark [3, 6].

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Defining the burden of community-onset BSI is needed to place its relative importance among other health conditions for setting health-care service and research funding priorities. We therefore conducted population-based surveillance in a large Canadian region in order to define the overall and species-specific incidence of, and the associated hospital-related morbidity and mortality associated with, community-onset BSI.

PATIENTS AND METHODS

Study population

Calgary Health Region (CHR) is a health system that provides all medically necessary, publicly funded health care to the more than one million residents of Calgary, Airdrie and multiple nearby small towns, villages, and hamlets in a total area of more than 37 000 km² [12]. CHR has four major acute care institutions (total 1900 acute care beds) and eight rural health centres (total 145 acute care beds) that provide all of the acute in-patient care within the region [13]. All residents of CHR with identified community-onset BSI during the 5-year period between 1 January 2000 and 31 December 2004 were included in the study. Patients were deemed to be CHR residents if their listed residence was within the currently defined boundaries of CHR [12, 14].

Population-based surveillance

An active, population-based, laboratory surveillance design was utilized [15, 16]. All bloodstream infections occurring among CHR residents were identified by the regional laboratory, Calgary Laboratory Services (CLS), that performs nearly all (>95%) standard microbiology testing from hospitals, nursing homes, physicians' offices, and community collection sites in CHR. Basic demographic, hospital length of stay, and mortality outcome information was obtained through a linkage with the CHR Data Warehouse, a large administrative database that maintains information on all patients admitted to any of the four acute care institutions in CHR [16].

Laboratory procedures and definitions

All blood was cultured at CLS using the BacT/Alert automated instrument (Organon Teknika, Durham, NC, USA). A blood culture set consisted of an aerobic/anaerobic bottle pair of BacT/Alert FAN bottles obtained from a single draw [17]. Organisms were isolated and speciated using standard methods. A bloodstream infection was defined as the growth of a pathogenic organism from at least one set of blood cultures. Because of the difficulty in establishing their clinical significance, organisms frequently associated with contamination including coagulase-negative staphylococci, viridans group streptococci, or *Bacillus*, *Corynebacterium*, or *Propionibacterium* species were *a priori* excluded from analysis. Infections with the same organism in a given patient within a 1-year period were classified as a single incident case. Community-onset BSI were classified as those submitted from community-based collection sites or those identified within the first 2 days of admission to an acute care facility. Poly-microbial bloodstream infections were those that had more than one species isolated within a 2-day period.

Statistical analysis

All analyses were performed using STATA version 9.0 (StataCorp, College Station, TX, 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 specific to the April 2003 boundaries of CHR as the denominator and compared using Poisson counts. Age- and gender-specific risks were calculated and reported as risk ratios (RR) with 95% confidence intervals (CI) as previously described [18].

RESULTS

During the 5 years of surveillance, a total of 4467 episodes of community-onset BSI were identified among 4192 CHR residents for an overall annual incidence of 81·6/100 000 population. Ninety-two percent (4104/4467) of episodes of had the positive cultures submitted from one of the major acute care centres and the remainder were submitted from community-based sites. Two hundred and thirty-six (5%) patients had second incident episodes of bloodstream infection and 32 (1%) had three, six had four, and one patient had five episodes during the course of the study. There was moderate variability ($P=0{\cdot}02$) in the year-to-year incidence (/100 000) of 81·0 in 2000,

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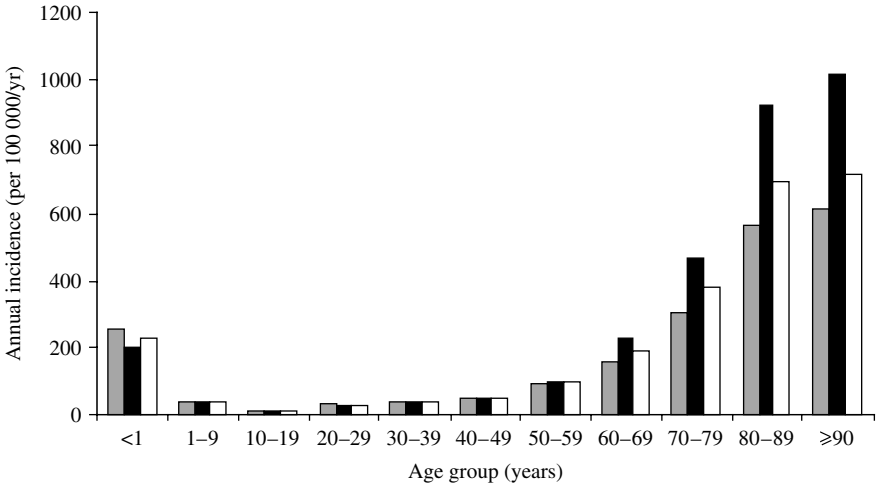

Fig. Age- and gender-specific incidence of community-onset bloodstream infections, Calgary Health Region, 2000–2004. ▒, Female; ■, male; □, total.

86·2 in 2001, 74·0 in 2002, 81·8 in 2003, and 84·8 in 2004.

Demographic risk factors

The median age was 61·8 (IQR 41·4–76·5) years and just more than half (51%, 2288) of episodes occurred in males. However, there was a dramatic relationship 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 the Figure. Although the overall annual incidence of community-onset BSI was comparable in males and females (83·7 *vs.* 79·3/100 000; RR 1·06, 95% CI 0·99–1·12, $P=0·07$); in those aged ⩾60 years, men were at significantly higher risk compared to women (396·1 *vs.* 292·5/100 000; RR 1·35, 95% CI 1·25–1·47, $P<0·0001$).

Major acute care hospital admission and outcome

Overall 3445/4467 (77%) episodes resulted in admission to one the four major regional acute care institutions, representing ∼0·7% of all admissions to these institutions. The subsequent hospital length of stay was a median of 9 (IQR, 5–15) days; the total days of acute hospitalization attributable to community-onset BSI was 51 146 days or 934 days/100 000 population per year. Among the 3445 episodes of community-onset BSI that required hospital admission, 460 were associated with in-hospital death for a case-fatality rate of 13% (95% CI 12·2–14·5). Among patients surviving to hospital discharge, the median length of stay was 9 days (IQR 6–15) and 119 were transferred to another acute care facility, 139 to a long-term care facility, and the remainder returned to the community.

Microbiology

Although a wide range of organisms caused community-onset BSI, the three species *Escherichia coli* (1414 isolates), *Staphyloccocus* (*S.*) *aureus* (737 isolates), and *Streptococcus* (*Str.*) *pneumoniae* (552 isolates) were responsible for the majority of cases. The relative occurrence of the most important infecting organisms varied by age; *E. coli*, *S. aureus*, and *Str. pneumoniae* were responsible for 35%, 9%, and 19% of infections in those aged <1 year, 11%, 17%, and 33% in those aged 1–19 years, 29%, 17%, and 13% in thoase aged 20–64, and 34%, 15%, and 7% in those aged ⩾65 years, respectively. Tables 1 and 2 compare the epidemiology characteristics and outcome of the ten most common species causing community-onset BSI in this study. Overall, 238 (5%) of episodes of community-onset BSI were of poly-microbial aetiology. Although poly-microbial infections were not associated with either gender or a higher rate of admission to hospital, as compared to mono-microbial bloodstream infections they were significantly associated with older median patient age (69·9 *vs.* 62·3 years, $P<0·001$) and a longer median hospital length of stay (10 *vs.* 9 days, $P=0·04$).

DISCUSSION

In this study we document the major burden of illness associated with community-onset BSI. We found that

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Table 1. *Comparison of the epidemiological characteristics of the ten most common causes of community onset bloodstream infection, Calgary Health Region, 2000–2004*

Species	*n*	Incidence (per 100 000 population)	Incidence (per 100 000 population)		Risk ratio (95% CI)	Poly-microbial	Median age (years)
			Male	Female			
Escherichia coli	1414	25·8	20·1	31·5	0·64 (0·57–0·71)	96 (7%)	66·2
Staphylococcus aureus	737	13·5	16·7	10·3	1·63 (1·40–1·90)	42 (6%)	60·4
Streptococcus pneumoniae	552	10·1	10·8	9·4	1·15 (0·97–1·37)	9 (2%)	44·4
Klebsiella pneumoniae	288	5·3	6·0	4·5	1·35 (1·06–1·71)	43 (15%)	70·0
Streptococcus pyogenes	178	3·3	3·8	2·6	1·46 (1·07–2·00)	8 (4%)	48·4
Enterococcus faecalis	156	2·9	3·6	2·1	1·70 (1·21–2·39)	33 (21%)	69·3
Bacteroides fragilis	132	2·4	2·2	2·6	0·84 (0·58–1·19)	27 (20%)	68·1
Streptococcus agalactiae	128	2·3	2·2	2·5	0·89 (0·62–1·27)	15 (12%)	54·7
Pseudomonas aeruginosa	109	2·0	2·3	1·7	1·37 (0·92–2·06)	27 (25%)	69·5
Proteus mirabilis	71	1·3	1·4	1·2	1·09 (0·67–1·79)	19 (27%)	77·0
Other	959	17·5	19·5	15·4	1·27 (1·12–1·45)	175 (18%)	60·3

CI, Confidence interval.

Table 2. *Admission to acute care hospitals and outcome associated with different aetiologies of community onset bloodstream infection, Calgary Health Region, 2000–2004*

Species	*n*	Number admitted	Median LOS (IQR) in days	In-hospital death
Escherichia coli	1414	1073 (76%)	8 (5–13)	96 (9%)
Staphylococcus aureus	737	578 (78%)	12 (7–26)	101 (17%)
Streptococcus pneumoniae	552	420 (76%)	8 (4·5–14)	52 (12%)
Klebsiella pneumoniae	288	243 (84%)	8 (6–14)	36 (15%)
Streptococcus pyogenes	178	138 (78%)	10 (6–23)	22 (16%)
Enterococcus faecalis	156	124 (79%)	10·5 (6–18·5)	14 (11%)
Bacteroides fragilis	132	112 (85%)	10 (6–20)	18 (16%)
Streptococcus agalactiae	128	103 (80%)	10 (6–16)	7 (7%)
Pseudomonas aeruginosa	109	92 (84%)	8 (5–18)	28 (30%)
Proteus mirabilis	71	57 (80%)	9 (6–16)	7 (12%)
Other	959	714 (74%)	9 (5–15)	126 (18)

LOS, Length of stay; IQR, interquartile range.

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 ~1 day/100 residents per year, and is associated with the deaths of more than 1/10 people infected. It must be recognized that bloodstream infection 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 infections will have different clinical courses and outcomes. In addition, the establishment of its incidence is dependent on the decision to draw samples of blood for culturing. While no specific protocols for blood culturing practices exist in CHR, others have noted that with diseases of higher severity, clinicians tend to be fairly uniform in their decision to send cultures [19].

Unlike with other designs where the base population at risk may not be defined, population-based studies conducted within well-defined boundaries have the advantage that if denominator data are available incidence rates may be determined [7]. Population incidence rates allow meaningful like-comparison of relative impact across a number of health-related conditions. We found that the incidence of bloodstream infection was 82/100 000 population and that 13% suffered in-hospital death. These numbers compare with recent population-based data from Alberta assessing major traumatic injury (70/100 000 per year; 12% in-hospital death),

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myocardial infarction (incidence 161/100 000 per year; in-hospital case-fatality 9% in 1999), and stroke (150/100 000 per year; 13% in-hospital death) among adults [20–22]. These data demonstrate that bloodstream infection is an important cause of morbidity and mortality and provides supportive rationale for leveraging of limited health-care and clinical research resources.

We observed that *Escherichia coli* (30%), *S. aureus* (16%), and *Str. pneumoniae* (12%) were the most important agents of community-onset BSI. Pedersen *et al.* also found that *E. coli* (605 episodes, 33%) was the most important aetiology of community-onset bacteraemia in their population-based study conducted between 1992 and 1997 in North Jutland, Denmark [6]. However, they observed a proportionally much higher rate of *Str. pneumoniae* disease (400 episodes, 22%) and lower rate of *S. aureus* infections (145 episodes, 8%) as compared with our study. They did not report population-based incidence rates for direct comparison. Our rate of community-onset *S. aureus* bloodstream infection of 14/100 000 was slightly less than observed in the United States in 1998 of 17/100 000 population [10] and our rate of pneumococcal bloodstream infection of 10/100 000 is similar to that observed in multiple other population-based studies worldwide [23–25]. Despite it being the most important cause of community-onset BSI, there is a paucity of studies investigating *E. coli* bloodstream infections in non-selected populations. Madsen *et al.* conducted population-based surveillance in North Jutland, Denmark from 1981 to 1994 and found an incidence of *E. coli* bacteraemia of ~32/100 000 [3].

It is notable that 23% of patients in this study did not have evidence of admission to a major acute care centre in CHR. Although a similar rate of outpatient management of community onset *E. coli* bloodstream infections has recently been reported from the United States [9]; based on our clinical experience we suspected that this number would have been closer to 15%. If in fact the true rate is lower than we observed, one possibility is that patients were managed through other means including admission to smaller local or extra-regional hospitals that were not included in our administrative database [13]. Given that the four major acute care centres represent ~95% of the acute care bed capacity in the region, this possibility would be expected to account for no more than 5%. Since CHR is relatively geographically isolated with the next major medical centres hundreds of kilometres away, it is likely that few patients would have been managed at non-regional hospitals. A second major reason for the potentially low admission rate observed could be that patients who were initially stabilized in an emergency department were subsequently managed through our outpatient parenteral therapy clinics. These clinics are based at each of the four major acute care centres, see thousands of new patients yearly, and readily accept acute patients from the emergency departments in less than 24 h of referral [26]. A third possibility is there was linkage failure with the microbiology and administrative databases. We hand searched a random sample of non-admitted cases and indeed found that ~5% of admissions failed to be identified by our linkage strategy. Fourth, we included residents of nursing homes as community-onset disease in this study and it is possible that some of these residents were treated at their facilities. Unfortunately, we do not have specific data on this population. While each of these possibilities are important potential biases, it is relevant that they would probably result in an underestimation of the true impact of community-onset BSI. The substantial morbidity and mortality rates we report in this study should therefore be viewed as conservative.

In conclusion, we report important and novel population-based surveillance of community-onset BSI and demonstrate their major impact. We identified that these infections are common, that the very young and old are at highest risk, that they result in admission to hospital for long periods of time, and many patients die as a result. Community-onset BSI are an important cause of morbidity and death. Documenting this major burden of disease should be important to promote further preventive efforts and to argue for increased funding for clinical research aimed at reducing the impact of these infections.

DECLARATION OF INTEREST

None.

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