Population-Based Study of the Epidemiology and the Risk Factors for *Pseudomonas aeruginosa* Bloodstream Infection

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Abstract

Background: Detailed population-based data on the epidemiology of *Pseudomonas aeruginosa* bloodstream infections are sparse. We sought to describe the incidence rate, risk factors, and outcomes associated with *P. aeruginosa* bacteremia in a large Canadian health region.

Patients and Methods: A retrospective population-based surveillance for *P. aeruginosa* bacteremia was conducted in the Calgary Health Region (CHR, population: approx. 1.2 million) during the period from 2000 to 2006.

Results: A total of 284 incident cases of *P. aeruginosa* bacteremia were identified in CHR residents, corresponding to an annual incidence rate of 3.6/100,000. Nosocomial acquisition accounted for 45% of cases, healthcare-associated community onset for 34% of cases, and community-acquired (CA) cases for 21%. Relative to the general population, risk factors for bloodstream infection included male sex, increasing age, hemodialysis, solid organ transplant, diagnosis of cancer, heart disease, HIV infection, diabetes mellitus, and/or chronic obstructive airway disease (COPD). Overall mortality was 29%. Factors associated with mortality in univariate analysis included pulmonary focus of infection and co-morbidities, including chronic liver disease, substance abuse, heart disease, COPD, and cancer, and increased with the burden of co-morbidities. Despite those patients with CA disease having fewer co-morbidities, they had a significantly higher mortality rate than either healthcare-associated cases or nosocomial cases (RR 1.88, p = 0.05).

Conclusions: This study documents that *P. aeruginosa* bacteremic disease is responsible for a significant burden of illness in general populations and identifies those groups at increased risk of infection and subsequent mortality. This information can be used to identify those individuals likely to benefit from empiric anti-pseudomonal therapies.

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Introduction

Pseudomonas aeruginosa bacteremia is associated with the one of highest mortality rates among bacterial nosocmial blood stream infections (BSIs) (18–61%) [1–14]. While numerous series have been published describing risk factors associated with *P. aeruginosa* bacteremia, these have mainly been restricted to community [13] and tertiary care referral hospitals [6, 10–12, 14, 15] or to special populations, such as pediatric patients [16], patients in intensive care units [17, 18], cancer patients [8, 9], or transplant recipients [19]. Few unselected studies of invasive *P. aeruginosa* have been conducted. Those studies that have been carried out have been largely descriptive and not compared incident risk factors in *P. aeruginosa* bacteremic patients relative to the general population [4, 20–22].

Population-based studies are the optimal approach to quantify trends in the occurrence, clinical characteristics, risk factors, and outcome of infectious diseases [23, 24]. Using these modalities, all episodes of disease occurring in a defined area can be ascertained, thereby minimizing selection bias inherent to less rigorous studies. By analyzing the occurrence of an infection in the context of the

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known distribution of select diseases in a defined population, proper incidence rates may be calculated to determine the risk of individual variables [24, 25]. Only recently have population-based studies investigating the epidemiology of bacteremic *P. aeruginosa* infections been reported [22, 26]; however, analyses of risk factors for invasive disease have been limited. The objective of this study was to conduct a population-based surveillance in a large unselected population in order to define the incidence of and determine the risk factors for *P. aeruginosa* bacteremia. We sought to determine if traditionally recognized risk factors for invasive disease and subsequent mortality would be confirmed with a more rigorous study design.

Methods

Study Population

The Calgary Health Region (CHR) administers virtually all medical and surgical care to residents of Calgary, Alberta and the surrounding area (population 1.2 million). A detailed description of the CHR is available through a regional website [27]. Only those patients requiring acute surgery for liver, heart, or lung transplantation are referred elsewhere. After acute transplant surgical issues have been resolved, continued care occurs in the CHR. All persons residing in the CHR who developed *P. aeruginosa* bacteremia from January 1, 2000 to December 31, 2006 were included in the study. Ethical approval for this study was granted by the Conjoint Health Research Ethics Board at the University of Calgary and the CHR.

Study Protocol

This study utilized an active, population-based surveillance cohort design to identify bacteremic *P. aeruginosa* infections in the CHR. Surveillance was conducted by Calgary Laboratory Services (CLS), a regional centralized laboratory system which processes ≥ 95% of blood samples in the area. Detailed demographic and outcome information was obtained on all patients admitted to any of the four major acute care hospitals using ICD 9 codes available from the regional corporate data warehouse.

Definitions

All blood samples were cultured using the BacT/Alert automated instrument (Organon Teknika, Durham, NC). *P. aeruginosa* BSI was defined by its isolation from one or more sets of blood culture bottles collected using standard sterile techniques. All isolates were deemed clinically significant. Clinical isolates were confirmed as *P. aeruginosa,* and tested for antimicrobial susceptibility by standard techniques [28]. The presence of metallo-beta-lactamases (MBLs) was evaluated in imipenem-resistant strains using both an EDTA screen test and the MBL E-test (AB BioDisk, Solna, Sweden) in accordance with the manufacturer's instructions [29, 30].

Residency status was established using the 2003 boundaries of the CHR [27]. Detailed population census data determined yearly were used to calculate incidence rates. Incident cases were defined by the first isolation of *P. aeruginosa*. Repeat isolation within 365 days was deemed to represent recurrence. Nosocomial bacteremias were defined as those where the first positive culture was obtained ≥ 48 h after admission or ≤ 48 h after discharge. Community onset (CO) infections were those where the first positive culture was obtained < 48 h after admission or > 48 h after discharge from the hospital. These categories were further subdivided into healthcare-associated community onset (HCA-CO) and community-acquired (CA) infections [31]. HCA-CO *P. aeruginosa* bacteremia was characterized by at least one of the following: (1) the patient had attended a specialized hospital clinic or emergency room within the preceding 2–30 days before BSI, (2) the patient had been admitted to a CHR acute care hospital for 2 or more days within the prior 90 days before BSI, (3) the patient was a resident of a nursing home or long-term care facility, or (4) the patient was on outpatient hemodialysis. Data on dialysis were not available for children. CA infections were a diagnosis of exclusion and included only those CO bacteremias that did not meet criteria for HCA-CO. For each patient, a primary diagnosis of the source of *P. aeruginosa* infection was made using discharge codes and cultures obtained within 48 h of the index incident blood culture draw.

Statistical Analysis

Analysis was performed using Stata ver. 10.0 (Stata Corp, College Station, TX). Non-normally distributed variables were reported as medians with inter-quartile ranges (IQR) and compared using the rank sum test. Differences in proportions among categorical data were assessed using Fisher's exact test for pair-wise comparisons and the chi-square test for multiple groups. The incidence of *P. aeruginosa* bacteremia was calculated by dividing the number of incident cases by the defined regional population at risk [32]. Risk factors for developing *P. aeruginosa* BSI were quantified as previously described [23]. The population at risk was ascertained or estimated using local patient registry data (HIV, dialysis, and transplant) [33–35], regional or Canadian survey data (alcoholism, cancer, and other medical co-morbid illnesses, including heart disease as defined as ischemic heart disease and/or congestive heart failure) [27, 36], or published North American epidemiology studies (inflammatory bowel disease, rheumatoid arthritis, and systemic lupus erythematosus) [37–39]. Risks were expressed as incidence rate ratios (RR) and reported with 95% confidence intervals (CI). Mortality rates were calculated using all-cause hospital deaths. A logistic regression model was developed to identify independent factors associated with mortality. Factors associated with death in univariate analyses ($p \leq 0.2$) were included, and backward variable

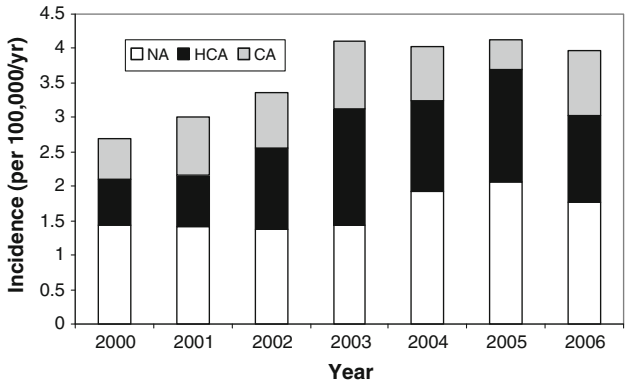

Figure 1. Annual incidence of *P. aeruginosa* bloodstream infection in the Calgary Health Region, 2000–2006. NA: Nosocomial acquired; HCA: healthcare-associated community acquired; CA: community acquired.

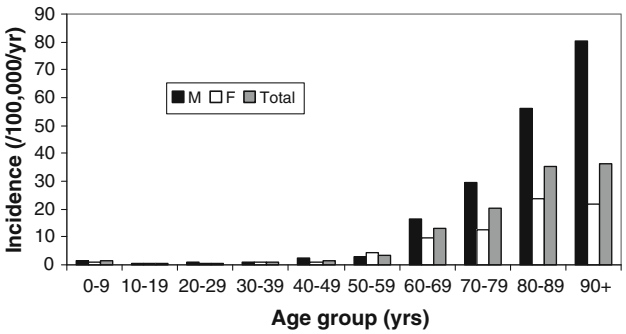

Figure 2. Age and gender related incidence of *P. aeruginosa* bacteremia, Calgary Health Region, 2000–2006. F: Female; M: male.

elimination was used to create the most efficient model. Calibration of the final model was assessed using the Hosmer-Lemeshow goodness-of-fit test. Discrimination was assessed using the area under the receiver operator curve. Model results are reported as odds ratios (OR) with 95% CI. For all statistical comparisons a p-value ≤ 0.05 was deemed significant.

Results

During the 7-year study, 284 CHR residents had at least one incident of *P. aeruginosa* BSI; one patient had two and one patient had three incident episodes. Basic demographic (age, gender, residency) and microbiologic data were available for all patients. Detailed outcome information was available for the 260/284 (92%) cases managed at one of the four major acute care centers, and co-morbidity information was available for 249/284 (88%). Among the 284 incident *P. aeruginosa* BSI, 128 (45%) were classified as nosocomial, 96 (34%) as HCA-CO, and 60 (21%) as CA. Among the HCA-CO cases, 35 (36%) had been recently managed in an emergency room setting (ER) or specialized hospital clinic, 64 (67%) had been recently hospitalized, eight (8%) were dialysis patients, and 18 (19%) were nursing home or long-term care facility residents.

Incidence and Risk Factors

The overall annual incidence rate of *P. aeruginosa* bacteremia was 3.6/100,000 population. Incidence rates increased during the first 4 years of the study in correlation with increases in HCA-CO and nosocomial acquired disease and then stabilized thereafter, as shown in figure 1. The incidence of *P. aeruginosa* BSI increased with advancing age, as shown in figure 2. The median age was 68.5 years (IQR 54.6–77.6) and was not different for CA cases (68.5 years; IQR 55.5–75.3) as compared to nosocomial (65.9 years; IQR 49.5-76.6) and HCA-CO (68.4 years; IQR 52.7–80.1) infections. Males were at increased risk for *P. aeruginosa* bacteremia (RR 1.52, IQR 1.20–1.93, $p < 0.0001$).

Most individuals bacteremic with *P. aeruginosa* had one or more documented co-morbidities (227/249, 92%). Those individuals with CA disease were more likely to have no prior co-morbidities (9/40, 22.5%) than those with either nosocomial (5/122, 4%) or HCA-CO disease (4/83, 5%) ($p < 0.001$). A number of selected conditions were assessed as risk factors for acquiring *P. aeruginosa* BSI, and these are shown in table 1. Those risk factors most strongly associated with bacteremia were hemodialysis, cancer, solid organ transplantation, heart disease, HIV infection, and diabetes. Among the 114 patients with cancer, 56 (49%) had hematologic malignancies, 58 (51%) had solid organ malignancies, and 67 (59%) were receiving chemotherapy. Eight infections occurred amongst solid organ recipients: one heart, three liver, three kidney, and one combined kidney–liver transplant. The distribution of co-morbidities relative to presentation classification is shown in table 2.

Susceptibility testing results were available for 267 (94%) of isolates. The rates of non-susceptibility to the standard anti-pseudomonal agents was 9% to piperacillin, 5% to piperacillin–tazobactam, 17% to ceftazidime, 12% to imipenem, 18% to ciprofloxacin, 16% to gentamicin, and 8% to tobramycin. Resistance rates remained stable for imipenem, gentamicin, tobramycin, ciprofloxacin, and ceftazidime over the 7 years of the study. However, an increase in piperacillin non-susceptibility was observed during this period ($p = 0.02$).

Multi-drug resistance (MDR), as defined by resistance to two or more classes, occurred in 44 cases (16%). The risk for MDR pathogens was associated with the source of acquisition ($p < 0.001$). Relative to CA cases, nosocomial cases were associated with a 13.55 RR (IQR 1.89–96.6) and HCA-CO cases with a 7.2 RR (IQR 1.0–54.67) of MDR *P. aeruginosa*. MDR was observed to increase over time during the study and then to trail off in the last year of the study ($p = 0.04$). Fourteen (5.4%)

Table 1
Risk for *P. aeruginosa* bacteremia associated with selected underlying conditions.

Factor	Age group	Patients with PABSI (n = 249)	Annual incidence per 100,000	Relative risk (95% CI)	p-value
Hemodialysis	20+	15	521	123.26 (73.26–207.38)	< 0.0001
Cancer	20+	111	107	46.18 (35.86–59.46)	< 0.0001
Solid organ transplant	20+	8	187	44.35 (21.94–89.63)	< 0.0001
Heart disease	12+	90	36	14.24 (11.00–18.43)	< 0.0001
HIV infection	All	2	37	11.56 (2.87–46.45)	0.01
Diabetes mellitus	12+	50	25	8.06 (5.94–10.95)	< 0.0001
Stroke	12+	13	21	5.95 (3.47–10.20)	< 0.0001
COPD	12+	36	19	5.70 (4.02–8.08)	< 0.0001
Crohn's disease	All	3	14	4.30 (1.38–13.41)	0.03
Alcoholism	20+	12	5	1.29 (0.74–2.25)	0.33
SLE	20+	1	1	1.11 (0.15–7.92)	0.59
Hepatitis C	All	1	1	0.44 (0.06–3.16)	0.73
Rheumatoid arthritis	20+	1	2	0.41 (0.06–2.93)	0.74
Asthma	12+	4	1	0.22 (0.08–0.59)	0.0002

Incidence rate in population at risk determined from registry data (some data having age limitations); PABSI: *P. aeruginosa* blood stream infection; COPD: chronic obstructive pulmonary disease; SLE: systemic lupus erythematosus; CI: confidence interval

Table 2
Distribution of co-morbidities in patients diagnosed with bacteremic *P. aeruginosa* infections.

Co-morbidities	Total number	Nosocomial (%)	Healthcare-associated (%)	Community acquired (%)
Hemodialysis	18	9 (50)	9 (50)	0
Cancer	114	57 (50)	41 (36)	16 (14)
Solid organ transplant	8	6 (75)	1 (13)	1 (13)
Heart disease	90	54 (60)	25 (27)	11 (13)
HIV infection	2	1 (50)	1 (50)	0
Diabetes mellitus	50	25 (50)	22 (44)	3 (6)
Stroke	13	5 (38)	7 (54)	1 (8)
COPD	36	21 (58)	12 (33)	3 (8)
Crohn's disease	3	2 (67)	1 (33)	0
Alcoholism	12	8 (67)	2 (17)	2 (17)
SLE	1	0	1 (100)	0
Hepatitis C	1	0	1 (100)	0
Rheumatoid arthritis	1	0	1 (100)	0
Asthma	4	2 (50)	2 (50)	0

isolates produced a MBL. Acquisition of an MBL-producing *P. aeruginosa* was strongly associated with increasing contact with the healthcare system: 11/117 (9.4%) nosocomial isolates produced an MBL, while only 3/84 (3.6%) HCA-CO isolates and 0/45 (0%) CA isolates produced an MBL (p = 0.05). The only co-morbidity significantly associated with MBL BSI was cancer (10/104 [10%] vs 3/128 [2%]; 4.10 RR, 95% CI 1.16–14.52, p = 0.02). Whereas MBL isolates were not observed from 1999 to 2003, they remained endemic in the subsequent period, comprising 6.6–15% of *P. aeruginosa* BSI isolates each year.

Clinical Characteristics of *P. aeruginosa* Bacteremic Patients and Outcome

A respiratory source of *P. aeruginosa* BSI was the most common, followed by primary bacteremia and urinary etiologies (Table 3). The time from admission to development of nosocomial BSI was a median of 13.6 days (IQR 6.7–22.6). Time to discharge was longest for nosocomial cases, 13.9 days (IQR 2–33.4), shorter for HCA-CO cases, 10.2 days (IQR 5–21, p = 0.23), and shortest for CA cases, 4.9 days (IQR 1.5–8.4, p = 0.0002). MDR isolates were more likely to be associated with prolonged hospitalization than non-MDA isolates: 36 (IQR 6–36) vs 14 days (IQR 17–58), respectively (p < 0.0001).

Overall mortality was 76/259 (29%). Co-morbidities associated with risk of death are included in table 4. The increasing burden of co-morbidities was associated with an increased risk of death (Figure 3), with the highest mortality observed in CA infections (16/43, 37%; 1.88 RR, IQR 1.06–3.35, p = 0.05) followed by nosocomial (42/126, 33%; 1.68 RR, IQR 1.03–2.76) relative to HCA-CO (17/86, 20%) infections. Mortality was greatest in individuals with a pneumonic origin of bacteremia (34/81, 42% vs 42/168, 25%; 1.68 RR, IQR 1.16–2.42, p = 0.008), and least in individuals bacteremic from a urinary source

Table 3
Primary diagnoses of bacteremic *P. aeruginosa* infections.

Primary diagnosis (n = 249)	Total number (%[a])	Nosocomial	Healthcare-associated	Community-acquired
Primary bacteremia	52 (20.8)	26	17	9
Skin and soft tissue [a]	21 (8.4)	10	7	4
Respiratory	81 (32.5)	48	22	11
Endovascular	8 (3.2)	3	5	0
Intrabdominal/pelvic	19 (7.6)	10	4	5
Urinary	50 (20.1)	19	23	8
Hepatobiliary	14 (5.6)	5	4	5
Other [b]	4 (1.6)	3	1	0

[a] Including three episodes secondary to burn infections; [b] others include one bone and joint infection, two CNS infections, one transfusion-associated infection

Table 4
Univariate analysis of co-morbidities associated with death in *P. aeruginosa* bacteremia.

Factor	Mortality with factor (%)	Mortality without factor (%)	Relative risk (95% CI)	p-value
Chronic Liver disease	10/18 (55.6)	66/231 (28.6)	1.94 (1.23–3.08)	0.03
COPD	18/36 (50)	58/213 (27.2)	1.84 (1.24–2.72)	0.01
Any cancer	44/114 (38.6)	32/135 (22.3)	1.63 (1.11–2.38)	0.013
Solid organ malignancies	28/58 (48.3)	48/191 (25.1)	1.92 (1.34–2.76)	0.001
Breast cancer	5/8 (62.5)	71/241 (30)	2.12 (1.20–3.76)	0.05
Lung cancer	8/15 (53.3)	68/234 (29.1)	1.84 (1.10–3.07)	0.05
Hematologic malignancies	16/56 (28.6)	60/193 (31.1)	0.96 (0.80–1.17)	0.87
Heart disease	36/90 (40)	40/159 (25.2)	1.59 (1.10–2.30)	0.02
Trauma	12/31 (38.8)	64/218 (29.3)	1.32 (0.81–2.15)	0.30
Age > 70	38/116 (32.7)	38/143 (26.6)	1.23 (0.85–1.79)	0.33
Diabetes mellitus	17/50 (34)	59/199 (29.6)	1.14 (0.74–1.78)	0.61
Allogeneic stem cell transplant	1/4 (25)	75/245 (30.6)	0.82 (0.15–4.51)	1.00
Solid organ transplant	2/8 (25)	74/241 (30.7)	0.81 (0.24–2.74)	1.00
Male sex	40/155 (25.8)	36/105 (34.3)	0.75 (0.51–1.09)	0.16
Dementia	5/23 (21.7)	71/226 (31.4)	0.69 (0.31–1.54)	0.48
Chronic renal failure	8/38 (21)	68/211 (32)	0.65 (0.34–1.25)	0.19
Hemodialysis	4/13 (30.8)	71/242 (29.3)	1.05 (0.45–2.43)	1.00
Prior stroke	2/13 (15.4)	74/236 (31.3)	0.49 (0.14–1.78)	0.35
Autoimmune disease	1/7 (14.3)	75/242 (31)	0.46 (0.07–2.86)	0.68
Chronic genitourinary disease	7/45 (15.6)	69/209 (33.8)	0.46 (0.23–0.93)	0.02
Age < 18 years	1/15 (7)	75/259 (30.7)	0.22 (0.03–1.45)	0.07
HIV	0/2 (0)	76/247 (30.7)	–	1.00

(67/50, 14% vs 69/199 34.7%; 0.40 RR, IQR 0.20–0.82, p = 0.006). Characteristics of the hospitalization associated with increased risk of death included acute renal failure (28/56, (50% vs 48/193, 24.9%; 2.01 RR, IQR 1.40–2.88, p = 0.0005) and requirement for ICU admission (32/69, 46.4% vs 46/190, 24.2%; 1.92 RR, IQR 1.34–2.74, p = 0.001). Only piperacillin non-susceptibility was associated with death (10/20, 50% vs 48/191, 25.1%; 1.99 RR, IQR 1.20–3.29, p = 0.03). Neither the production of MBL (5/14, 35.7% vs 71/245, 29%; 1.23 RR, IQR 0.59–2.56, p = 0.56) nor MDR status (12/41, 29.2% vs 63/214, 29.4%; 0.99 RR, IQR 0.59–1.67, p = 1.00) were associated with death. Multivariate logistic regression was used to assess risk factors for death (Table 5). The final model (n = 249) included increasing age, acute renal failure, and co-morbidities, including heart disease, chronic liver disease, cancer, or non-urinary source of BSI.

Discussion

We report here population-based data describing the incidence, risk factors for, and outcome of *P. aeruginosa* bacteremia in a large non-selected North American population (approx. 8 million person-years of observation). Few previous studies have attempted to quantify the incidence of *P. aeruginosa* BSI. Those hospital-based studies that have been performed suggest this is a uncommon event, representing 0.39–4.7 cases/1,000 admissions [3, 6–9, 13, 14, 17]). The considerable variation in rates demonstrates the importance of population-based studies, as these other series are subject to influence by a number of variables, including differences in hospital expertise and referral patterns. In contrast, population-based studies are able to identify all individuals in a defined population, thereby minimizing bias allowing for a more valid analysis of disease incidence and distribution.

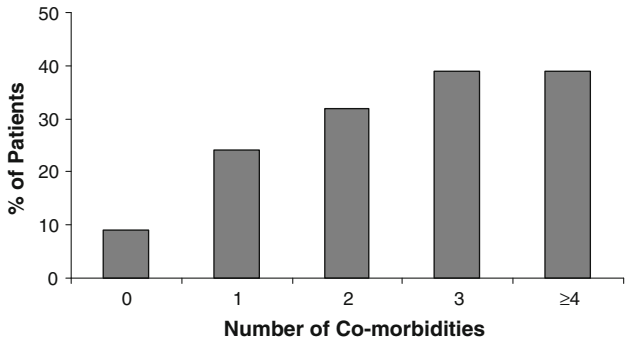

Figure 3. Increasing burden of co-morbidities in *P. aeruginosa* bacteremic individuals is associated with increased risk of death (p = 0.02).

Table 5
Logistic regression modeling of risk factors for mortality in patients with *P. aeruginosa* bacteremia.

Variable	Odds ratio (95% CI)	p-value
Chronic liver disease	3.83 (1.30–11.29)	0.02
Acute renal failure	3.16 (1.60–6.24)	0.001
Cancer	3.04 (1.60–5.76)	0.001
Heart disease	2.06 (1.08–3.92)	0.03
Age [a]	1.02 (1.00–1.04)	0.03
Urinary source	0.29 (0.11–0.73)	0.01

The final model (n = 249) had good calibration (goodness of fit p = 0.73) and discrimination (area under ROC curve = 0.77); [a]As compared with reference category of < 18 years of age

Two population-based studies of bacteremic *P. aeruginosa* have recently been reported in which incident rates of *P. aeruginosa* BSI were similar to that reported herein (3.6/100,000 person years) [22, 26]. *Al-Hasan* et al. reported an incidence rate of 6.4/100,000 in Olmstead County residents in their study limited to 69 incident episodes occurring in patients attending either the Mayo Medical Center or Olmstead Medical Center. Owing to the limited sample size, the analysis was restricted to demonstrating the increasing incidence with age and male sex, whereas the contribution of co-morbidities was not assessed. *Iversen* et al. [26] reported nation-wide data from Norway on 1,174 episodes occurring over 11 years identified by 22 different laboratories for an incidence rate of *P. aeruginosa* BSI of 2.43/100,000. However, this study was limited by the inclusion of *P. aeruginosa* and all other *Pseudomonas* spp. not identified at the species level, incomplete data from a minority of contributing laboratories, and reliance on physician-reported questionnaires.

Our study is the first to perform a detailed assessment of risk factors for *P. aerugions* BSI relative to a general population. The major risk factors associated with *P. aeruginosa* BSI identified in this study included increasing age, male sex, hemodialysis, solid organ transplantation, cancer, HIV infection, diabetes, and underlying chronic obstructive pulmonary disease (COPD). While many of these factors have been identified in other descriptive hospital-based series, the contribution of each was found to vary in these studies depending on the patient series examined, as determined by referral bias [6, 9, 40]. Furthermore, the magnitude of each individual risk is now apparent. While our analysis is important as it identifies and quantifies the actual risk of each factor in the population for acquisition of *P. aerugionsa* bacteremia, it is a limitation that we were not able to assess independent risk factors for the acquisition of *P. aeruginosa* disease using logistic regression. The reason for this is that we estimated the rates of underlying illnesses in the population at large but did not have individual linked data on all 1.2 million residents of the CHR. This limitation is nearly universal to all population-based observational designs [41, 42]. Another notable limitation to our study is our reliance on registry data that had restricted age ranges (commonly excluding children) for determining the prevalence of medical co-morbidities in the general population. This may have resulted in an underestimation of the true risk for certain conditions. However, as pediatric cases represented only 5% of cases, this difference is likely to be minimal. Lastly, we identified solid organ transplant as a significant risk for *P. aeruginosa* BSI (RR 44), this does not include data for the immediate period post-procedure and likely underestimates the true burden of this risk factor.

Encouragingly, antibiotic non-susceptibility was not observed to significantly increase over time, with the exception non-susceptibility to piperacillin. This result is in agreement with published data from large multi-center collaborations [43, 44]. Resistance to standard anti-pseudomonal agents was observed to increase with increasing contact with the healthcare system. However, antibiotic non-susceptibility was not associated with increased risk of death, with the exception of piperacillin [11, 45, 46], although it was associated with increased length of stay. We observed MDR in 16% of isolates in this series, which is consistent with values reported in several other recently published series. Importantly, no increased risk of death was observed with MDR strains [11, 20]. Notably, MBL-producing *P. aeruginosa* were observed to emerge during the latter half of the study and persist at a stable rate. MBL *P. aeruginosa* BSI was much more common in patients being treated for cancers, in particular hematologic malignancies [47].

Considerable variation in *P. aeruginosa* BSI-associated mortality has been reported in recent series (18–61%) [4, 10, 11, 13, 40]. However in unselected patient series this mortality rate appears to be more stable at 30–40%, suggesting that bias exists in centers with specific medical focus [3, 4, 20]. The overall mortality in our population-based study of *P. aeruginosa* BSI of 29% is similar to that reported in two other population-based

series, which identified overall mortality rates of 26 and 35%, respectively [22, 26]. Previous hospital-based studies have identified severity of illness at presentation, hypotension, older age, renal failure, and pulmonary focus as factors increasing the risk of death [4, 10, 40]. In general, there was agreement between these prior studies and the data herein. A higher mortality rate associated with pneumonia as a source of *P. aeruginosa* BSI has been a consistent finding [4, 6, 8, 9, 11, 13, 48]. We observed an almost twofold increase in mortality in pulmonary sources of bacteremia. Individuals with pneumonia were more likely to have greater burden of co-morbid illnesses, but they were not more likely to have acquired resistant pathogens. As such, it is likely that impaired host defenses and the advanced debility of patients contributes to the excess burden of disease. In contrast to earlier series, we observed a lower mortality associated with *P. aeruginosa* bacteremia complicating hematologic malignancies relative to solid organ malignancies [8, 9]. This likely reflects the adoption of empiric antibacterial regimens covering Pseudomonas as first-line therapy in febrile neutropenic hematology patients.

Few studies have evaluated CA bacteremia with *P. aeruginosa* specifically. In the largest study reported, *Kang* et al. [15] describe a cohort (n = 39) largely consisting of HCA-CO infections – a distinction that is increasingly recognized. These authors report an associated 30-day mortality of 39% and suggest that this may in part be related to the low rate of appropriate initial therapy in this group (38%). Consequently, mortality was significantly increased in those patients with CA disease. This is in stark contrast to many other series. This information is particularly relevant as this group is less likely to have underlying co-morbidities, and their infecting organisms are less likely to be MDR. Taken together, these results suggest that the poorer outcome in this group is related to the lack of empiric anti-pseudomonal coverage in a patient group deemed to be at a lower risk of *Pseudomonas* infection. These data suggest that empirical antibacterial therapies which cover *Pseudomonas* should be considered for those patients with risk factors for invasive *P. aeruginosa* presenting from the community with severe septic shock.

P. aeruginosa BSI is responsible for a significant burden of illness in general populations. The use of a population-based strategy for analysis of the contribution of underlying risk factors for invasive *P. aeruginosa* disease ensures that those groups at increased risk of infection and subsequent mortality are readily identified. This information can be used to identify those individuals likely to benefit from empiric anti-pseudomonal therapies.

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