Enterococcal bacteremia in a tertiary care centre in Winnipeg

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OBJECTIVE: To review experience with enterococcal bacteremia before the emergence of vancomycin-resistant enterococcus at a tertiary care teaching hospital.
DESIGN: Retrospective chart review of episodes of enterococcal bacteremia identified through the clinical microbiology laboratory from January 1990 to December 1994. Antimicrobial susceptibilities were performed for all isolates and pulsed-field gel electrophoresis for genetic typing of selected strains.
RESULTS: One hundred and twenty-six episodes of bacteremia were identified in 109 patients: 108 *Enterococcus faecalis*, 13 *Enterococcus faecium*, four both *E faecalis* and *E faecium*, and one *Enterococcus durans*. Enterococcal isolates occurred with polymicrobial bacteremia in 62 (49%) episodes. The most common sites of infection were central venous catheters (45%) and the urinary tract (21%). Enterococcal bacteremia was usually nosocomially acquired (88%), and associated with older age, instrumentation, and prior or current antimicrobial therapy. Overall mortality was 22%, and 7.2% was partially or fully attributable to enterococcal bacteremia. Resistance to ampicillin, high level gentamicin and high level streptomycin were 0%, 32% and 31% for *E faecalis*, respectively, and 44%, 0% and 47% for *E faecium*, respectively.
CONCLUSIONS: During this review, the frequency and impact of enterococcal bacteremia at this institution was relatively limited. Isolates resistant to ampicillin and aminoglycosides were emerging, but differences in patient outcomes were similar for resistant and susceptible isolates.

Key Words: *Bacteremia, Nosocomial, Entercocci*

Bactériémie entérococcique dans un centre de soins tertiaires de Winnipeg

OBJECTIF : Passer en revue les cas de bactériémie entérococcique avant l'émergence de la résistance des entérocoques à la vancomycine dans un hôpital universitaire de soins tertiaires.
MODÈLE : Étude rétrospective des dossiers médicaux pour la recherche d'épisodes de bactériémie entérococcique identifiée par le laboratoire de microbiologie clinique de janvier 1990 à décembre 1994. Des tests de sensibilité aux antimicrobiens ont été pratiqués chez tous les isolats ainsi qu'une électrophorèse sur gel en champ pulsé pour le typage des gènes des souches sélectionnées.
RÉSULTATS : Cent vingt-six épisodes de bactériémie ont été identifiés chez 109 patients : 108 à *Enterococcus faecalis*, 13 à *Enterococcus faecium*, 4 à *E. faecalis* et *E. faecium* combinés, et un à *Enterococcus durans*. Les isolats d'entérocoques accompagnaient une bactériémie polymicrobienne dans 62 (49 %) épisodes. Les sites d'infection les plus

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fréquents étaient les cathéters veineux centraux (45 %) et les voies urinaires (21 %). La bactériémie entérococcique était habituellement d'origine nosocomiale (88 %), et associée à un âge plus avancé, à un monitorage effractif et à un traitement antibiotique antérieur ou en cours. La mortalité globale était de 22 %, dont 7,2 % était en partie ou totalement attribuable à une bactériémie entérococcique. La résistance à l'ampicilline, à un niveau élevé de gentamicine et à un niveau élevé de streptomycine était respectivement de 0 %, 32 % et 31 % pour *E. faecalis*, et respectivement de 44 %, 0 % et 47 % pour *E. faecium*.

CONCLUSIONS : Pendant cette étude, la fréquence et l'impact de la bactériémie entérococcique dans l'établissement en question était relativement limitée. Les isolats résistants à l'ampicilline et aux aminoglycosides étaient en émergence, mais les différences observées dans l'évolution clinique des patients ne permettaient pas d'établir une distinction entre les isolats sensibles ou résistants.

Enterococci are an important cause of nosocomial infections (1,2). In the United States between 1986 and 1989, enterococci were the second leading cause of nosocomial infections after *Escherichia coli*, and the third leading cause of bacteremia after coagulase-negative staphylococci and *Staphylococcus aureus* (1). There has been an increasing incidence of enterococcal bacteremia in health care settings (3-6). Risk factors for acquiring nosocomial enterococcal bacteremia include poor general health, long hospital stay, presence of vascular or urinary catheters, and prior surgery or administration of antibiotics (7-12). Concerns about enterococcal infections have been compounded by increasing antimicrobial resistance, particularly to ampicillin, aminoglycosides and vancomycin (12-17). Enterococcal bacteremia has been associated with high mortality, largely because of underlying comorbidities (18). In one study, mortality was higher among patients with bacteremia due to high level gentamicin-resistant strains of *Enterococcus faecalis* than among those infected with susceptible strains (19), although this association was not observed in other studies (20,21).

At the Health Sciences Centre, Winnipeg, Manitoba, a tertiary care centre, enterococci account for 4% of bacteremic isolates. *S aureus* and *E coli* are the most common blood isolates (12% and 7%, respectively). Infections caused by vancomycin-resistant strains have not been identified, and vancomycin-resistant enterococci (VRE) have only recently been introduced to this tertiary care facility. This study was conducted to describe the epidemiology of enterococcal bacteremia at this institution before the introduction of vancomycin-resistant strains to determine the occurrence of ampicillin and high level aminoglycoside resistance in infecting organisms and to explore risk factors for acquiring bacteremic enterococcal infections. This information may assist in the future development of programs for control of VRE.

PATIENTS AND METHODS

Institution and patient population: The Health Sciences Centre is a tertiary care teaching hospital with a bed capacity ranging from 830 to 1150 beds during the time of this retrospective review. All patients with enterococcal isolates recovered from blood cultures during a five-year period (January 1990 to December 1994) were identified for this review.

Data collection: Patients were identified through a blood culture log book maintained by the clinical microbiology laboratory. A chart review by one of the authors (TAAM) was performed with standardized data collection. Information collected included patient demographics, admitting diagnosis, comorbidities, onset of bacteremia relative to date of admission, surgery and other invasive procedures, type and duration of antibiotic use, presence of foreign devices, admission to intensive care units, complications, and outcome.

Microbiological methods: During the study, blood was cultured using the BacT/Alert automated system (Organon Teknika Inc). For some patients with suspected disseminated fungal infection, the Lysis Centrifugation System (Isolator, Wampole Laboratories, New Jersey) was also used. Species of enterococci were identified using the MicroScan system (Baxter Diagnostics Inc). Organisms recovered from blood cultures were stocked in skim milk at –70°C.

Isolates of enterococci recovered in the study were retrieved, and the identification of the organisms was verified using Dade Microscan dried overnight Gram-positive panels (California) and confirmed using methods described by Facklam and Collins (22). Tests for antibiotic susceptibility and beta-lactamase production were repeated. Susceptibility testing to ampicillin was performed using the disc diffusion method (BBL, Becton Dickinson Microbiology Systems) according to published guidelines (23). Susceptibility testing to vancomycin and high level resistance to gentamicin and streptomycin was performed using the agar screening method (Entero High level Aminoglycoside Resistance Quadrant Agar, PML Microbiologicals). Ampicillin resistance was demonstrated by a zone of inhibition of less than 17 mm. Vancomycin resistance was demonstrated by growth of the organism on Mueller-Hinton agar screening plates containing 6 g/mL of vancomycin. High level gentamicin and streptomycin resistance were demonstrated by growth of the organism on agar containing 500 g/mL and 2000 g/mL of gentamicin and streptomycin, respectively. The nitrocefin disc (BBL, Becton Dickinson Microbiology Systems) was used to test for beta-lactamase production. Pulsed-field gel electrophoresis (PFGE) was performed as described by Murray et al (24) and interpreted according to Tenover et al (25).

Definitions: Enterococcal bacteremia was considered nosocomial if patients met any of the following criteria: bacteremia developed 72 h or more after admission to hospital; the patient attended regular hemodialysis at the hospital as an outpatient; the patient had been hospitalized for at least 72 h in the preceding 30 days; or the patient developed enterococcal bacteremia within 72 h of admission to hospital, but clinical circumstances provided clear evidence of hospital acquisition.

The clinical significance of enterococcal isolation from

TABLE 1
Characteristics of patients with enterococcal bacteremia

	Number (% of patients)
Episodes/patients	126/109
Male	70 (64%)
Mean age SD, median (years)	45 26, 51
Less than 1 year	12 (11)
1-15 years	8 (7.3)
16-50 years	34 (31)
51-70 years	31 (28)
Over 70 years	24 (22)
Underlying illness	106 (97)
Diabetes mellitus	17 (16)
Renal failure	39 (36)
Hemodialysis	32 (29)
No dialysis	7 (6.4)
Immunosuppression	30 (28)
Malignancy	18 (17)
Alcoholism	8 (7.3)
Liver disease	4 (3.7)
Other	41 (38)
Prior surgery	53 (48)
Abdominal	24 (22)
Genitourinary	9 (8.3)
Other*	20 (18)
Instrumentation (n=111)	95 (87)
Central venous catheter	76 (70)
Indwelling urinary catheter	37 (34)
Prior 30 days	10 (9.2)
Endotracheal tube	26 (24)
Chest tube	3 (2.7)
Nephrostomy tube	3 (2.8)
Others†	21 (19)

**Includes coronary bypass, pericardial window, renal artery revascularization, total abdominal hysterectomy, therapeutic abortion, empyema decortication, open lung biopsy, laminectomy, calcaneal resection and cerebral ventricular drain insertion; †Includes suprapublic catheter, condom catheter, ureteric stents, colostomy, peritoneal dialysis catheters, surgical drains, tracheostomy, Leveen shunt, arteriovenous fistula cannulation and pericardial catheter*

blood was determined by the number of positive blood culture sets or bottles, the presence or absence of a potential source of enterococcal infection and by the patient's clinical status. If the organism was isolated from more than one blood culture obtained during the same illness, it was considered a true pathogen. If the organism was recovered from only one bottle of a single blood culture set, it was considered a pathogen if there was a potential source for the infection, eg, central venous catheter in place or bowel abnormality. Monomicrobial enterococcal bacteremia was defined as isolation of clinically significant *Enterococcus* species without any other clinically significant pathogens from blood. Polymicrobial enterococcal bacteremia was defined as the isolation of a clinically significant *Enterococcus* species and one or more other clinically significant pathogens from blood. Enterococcal bacteremia was considered primary the first time it was identified in a given patient or if it recurred at least two weeks after completing adequate therapy of a previous enterococcal bacteremia. If enterococcal bacteremia occurred within two weeks after therapy of a previous enterococcal bacteremia, it was considered a relapse.

The source of infection was determined on the basis of clinical evidence and recovery of enterococcus from the infected site. Central venous catheters were considered the source of infection if blood cultures obtained from the lumens contained the organism and the patient had no other source of infection, or if there was local evidence of infection. Absence of growth of enterococcus from the central venous catheter tip upon culture was considered to be strong evidence against central venous catheter infection as a source of bacteremia if the catheter was removed before or within 48 h of commencing antibiotic therapy.

Requirement for more intense care was defined as any escalation of medical care that was required primarily because of the enterococcal bacteremia. This included hospital admission of patients with community-acquired infections or those on chronic hemodialysis; transfer of the patient from the ward to the intensive care unit; or initiating or increasing hemodynamic or respiratory support (including therapy with inotropes and/or invasive monitoring) due to septicemia-related complications. Empirical antibiotic therapy was considered appropriate if any of the following were used: ampicillin, piperacillin, imipenem or vancomycin with or without an aminoglycoside.

Mortality of patients was classified into three categories: not attributable to the enterococcal bacteremia – death occurring as a result of the patient's underlying disease after or during adequate treatment of enterococcal bacteremia not complicated by any organ damage secondary to sepsis that could have accounted for death; partially attributable – death occurred as a result of septicemia with enterococcus and one or more other organisms (polymicrobial infection); or attributable – death occurred due to enterococcal septicemia with no other pathogens contributing (monomicrobial infection).

Data analysis: The unpaired *t* test and ANOVA were used to compare means for continuous data. The Kruskal-Wallis nonparametric test was used to compare means for continuous data that did not follow a normal distribution. Comparison of proportions (categorical data) was by ^{2} or Fisher's exact test for small expected values.

RESULTS

During the five-year study, 137 episodes of enterococcal bacteremia were identified in 120 patients. *E faecalis* was isolated in 116 (84.7%) episodes, *Enterococcus faecium* in 15 (11.0%), both *E faecalis* and *E faecium* in five (3.6%), and *Enterococcus durans* in one (0.7%) episode. In 11 (8.0%) episodes occurring in 11 patients, the enterococcal isolates were considered to be contaminants; the episodes included eight (6.9%) of the 116 isolates of *E faecalis*, two (13.3%) of the 15 isolates of *E faecium*, and one (20.0%) of the dual isolates of both species. Thus, 126 episodes of clinically significant bacteremia occurred in 109 patients. Primary bacteremia occurred in 111

TABLE 2
Number of enterococcal isolates, and total and bacteremia-related mortality by source of infection in 126 episodes of enterococcal bacteremia

Source of bacteremia	Number of episodes (%)	Number of *Enterococcus faecalis* (*Enterococcus faecium*) isolates		Mortality due to bacteremia (total mortality)
		Monomicrobial	Polymicrobial	
Central venous catheters	57 (45.2%)	34 (5)	23 (2)	2 (12)
Urinary tract infection	26 (20.6%)	9 (0)	17 (0)	2 (5)
Intra-abdominal focus	19 (15.1)	9 (1)	10 (6)	3 (6)
Wound infection	5 (4.0%)	1 (0)	4 (1)	0 (2)
Endocarditis	4 (3.2%)	4 (0)	0	0 (0)
Other catheters*	5 (4.0%)	1 (0)	4 (1)	0 (0)
Other†	7 (5.6%)	4 (1)	3 (0)	0 (1)
Unknown	3 (2.4%)	2 (0)	1 (0)	0 (2)

**Peripheral venous catheters, Leveen shunt and pericardial catheter; †Perirectal abscess (one patient), arteriovenous fistula (one patient), vertebral osteomyelitis postmyelogram (one patient), chorioamnionitis after premature rupture of membranes (one patient), endometritis post-therapeutic abortion (two patients) and mediastinitis postesophagectomy (one patient)*

of the 126 (88.1%) clinically significant bacteremic episodes, and 15 (11.9%) episodes were relapses. Ninety-eight (88.3%) of the 111 primary bacteremic episodes were nosocomial, and 13 (11.7%) were community acquired. The mean duration of hospitalization before onset of nosocomial bacteremia was 38 46 days (median 23, range one to 270 days).

At least one other bacteremic pathogen was isolated in 62 (49.2%) of the 126 episodes of true bacteremia. Other pathogens isolated included coagulase-negative staphylococci (n=31), *E coli* (n=11), *S aureus* (n=7), *Klebsiella* species (n=5), *Enterobacter* species (n=4), *Morganella* species (n=3), *Streptococcus agalactiae* (n=3), *Streptococcus viridans* (n=2), and one isolate each of *Streptococcus bovis*, *Providencia stuartii, Proteus mirabilis*, *Flavobacterium* species, *Stenotrophomonas maltophilia*, *Pseudomonas aeruginosa*, *Citrobacter* species, *Lecrercia adecarboxylata* and *Acinetobacter anitratus*. In addition, there were four isolates of *Bacteroides* species, one *Clostridium* species and three *Candida* species (one each of *Candida albicans*, *Candida tropicalis* and *Candida glabrata*).

Patient characteristics are presented in Table 1. Patients tended to be male and over 50 years of age, and had significant comorbidities. Surgery preceded about one-half of the 111 clinically significant primary bacteremic episodes, and the majority of patients had one or more types of invasive instrumentation. Of the 98 primary nosocomial bacteremic episodes, 36 (36.7%) were acquired in intensive care units, including 15 in medical, 10 in surgical, seven in neonatal and four in paediatric intensive care units. Thirty-one (31.6%) episodes occurred on general surgical (n=16) and medical (n=15) wards. A total of 11 (11.2%), eight (8.2%), seven (7.2%) and five (5.1%) episodes were acquired on the hemodialysis, hematology/oncology, obstetrics/gynecology and paediatric wards, respectively. The most common site for infection was the central venous catheter (45.2%), with the urinary tract being the second most common (20.6%) (Table 2). *E faecium* isolates were identified in individuals with central venous catheter infections and with an intra-abdominal source of infection, but not in individuals with urinary tract infection or endocarditis. Comparison of the patients with monomicrobial enterococcal bacteremia with those with polymicrobial enterococcal bacteremia showed no difference in mean age, number or type of underlying diseases, source of infection and number of nosocomially acquired infections.

In 81 (73.0%) of the 111 primary bacteremic episodes, patients received antibiotics before or were receiving antibiotics at the time of the onset of bacteremia. In 68 (61.3%) episodes, patients received antibiotics in the preceding six weeks. These included ampicillin, penicillin, cloxacillin or piperacillin in 29 episodes (26.1%); imipenem in 12 episodes (10.8%); aminoglycosides in 24 episodes (21.6%); cephalosporins in 12 episodes (10.8%); metronidazole in 18 episodes (16.2%); systemic antifungal agents in eight episodes (7.2%); and other antibiotics including ciprofloxacin, clindamycin or erythromycin in 18 episodes (16.2%). In 38 (34.2%) episodes, patients were receiving antibiotics at the onset of bacteremia. The antibiotics included ampicillin, penicillin, cloxacillin or piperacillin in six episodes (5.4%); imipenem in one episode (0.9%); aminoglycosides in five episodes (4.5%); cephalosporins in 11 episodes (9.9%); vancomycin in eight episodes (7.2%); trimethoprim/sulfamethoxazole in seven episodes (6.3%); metronidazole in eight episodes (7.2%); systemic antifungal agents in seven episodes (6.3%); and other antibiotics including ciprofloxacin, clindamycin, erythromycin or nitrofurantoin in seven episodes (6.3%).

Empirical antibiotic therapy was appropriate in 88 (80.0%) of 110 treated episodes. In the remaining 22 (20.0%) episodes, enterococci were not suspected as causative pathogens. Vancomycin was the most common antibiotic used for appropriate empirical (48 of 110; 43.6%) or definitive (57 of 114; 50.0%) therapy, with ampicillin second in frequency (18 of 110 [16.4%] and 49 of 114 [43.0%], respectively).

Septic shock developed in 18 (14.3%) of the 126 episodes of enterococcal bacteremia, persistent bacteremia for at least three days in seven (5.6%) episodes and relapse of bacteremia in 15 (11.9%) episodes. There was no significant difference in the occurrence of septic shock (six cases versus 12, respectively, P=0.10) between individuals with monomicrobial or polymicrobial bacteremia. Escalation of medical care was re-

quired in 46 (36.5%) of the 126 episodes of enterococcal bacteremia, and occurred with equal frequency in those with polymicrobial compared with those with monomicrobial infection (21 of 62 versus 25 of 64, respectively, P=0.54). Of the 32 infected hemodialysis patients, nine (28.1%) required admission to the hospital for therapy.

Relapsed urinary tract infection occurred in six (25.0%) of the 24 patients with a urinary tract source of infection and in three cases with bacteremia. Of the 77 patients who had central venous catheters at the time of bacteremia, 26 (33.8%) had the catheters removed or replaced; subsequent relapse was not observed in these individuals after antimicrobial therapy. In four patients, there was no note in the chart to indicate whether the catheter was removed. In 47 patients (61.0%), the central venous catheters were not changed or removed. Of these, four (8.5%) had persistent bacteremia for at least three days, and nine (19.1%) had a relapse of central catheter infection with bacteremia. Relapse occurred significantly more frequently (P=0.014) when the catheter was not removed.

Twenty-eight (22.2%) deaths occurred in 126 bacteremic episodes. Death occurred in one of 12 (8.3%) of patients less than one year of age, none of the eight who were age one to 15 years, seven of 34 (20.6%) who were age 16 to 50 years, 11 of 31 (35.5%) who were age 51 to 70 years and nine of 24 (37.5%) who were older than 70 years. Partially attributable or attributable mortality was similar for those with monomicrobial or polymicrobial bacteremia (four deaths versus five, respectively, P=0.74). Mortality in 19 episodes (15.1%) was due to the patients' underlying diseases and was not related to the enterococcal bacteremia. Mortality in three (2.4%) episodes was partially attributable to enterococcal bacteremia (all polymicrobial infection). Death was attributable to enterococcal bacteremia in six (4.8%) episodes. Total mortality was higher in patients treated for *E faecium* bacteremia compared with patients treated for *E faecalis* bacteremia (six of 13 versus 16 of 96, P=0.02), but there was no significant difference in the partially attributable and attributable mortality between the two groups (two of 13 versus three of 96, respectively, P=0.10). Attributable mortality was significantly higher for patients with monomicrobial enterococcal bacteremia who did not receive specific antimicrobial therapy than for patients who received antimicrobial therapy (three of nine versus three of 55, respectively, P<0.01).

The susceptibilities of enterococcal isolates to ampicillin, gentamicin, streptomycin and vancomycin are shown in Table 3. No vancomycin-resistant enterococci were isolated. All *E faecalis* isolates were susceptible to ampicillin, but 43.8% of *E faecium* isolates were resistant. None of the enterococcal isolates were beta-lactamase positive. All *E faecium* isolates were susceptible to high level gentamicin, whereas 32.1% of *E faecalis* isolates were resistant. All streptomycin-susceptible *E faecium* isolates (eight isolates) were ampicillin-susceptible, and all streptomycin-resistant isolates (seven isolates) were ampicillin-resistant. DNA typing of the streptomycin-resistant *E faecium* strains by PFGE demonstrated three different patterns (three isolates belonged to pattern A, two isolates to pattern B_1, one isolate to pattern B_2, and one isolate to pattern C.

TABLE 3
Antimicrobial susceptibility of clinically significant enterococcal isolates

	Percentage of isolates resistant	
Antibiotic	***Enterococcus faecalis* (n=111)**	***Enterococcus faecium* (n=17)**
Ampicillin	0.0	43.8
Vancomycin	0.0	0.0
High level gentamicin	32.1	0.0
High level streptomycin	31.1	46.7
High level gentamicin and streptomycin	24.5	0.0
Ampicillin and high level gentamicin	0.0	0.0
Ampicillin and high level streptomycin	0.0	46.7

When patients with primary monomicrobial high level gentamicin-resistant *E faecalis* infections (n=15) were compared with those with monomicrobial infections due to high level gentamicin-susceptible strains (n=35), the former group had a longer hospital stay (51 21 versus 41 28 days, respectively, P=0.005). There was, however, no difference in age (54 21 versus 41 28 years, respectively, P=0.11), the number or type of underlying chronic diseases (17 [100%] versus 38 [95%], P=1), development of septic shock (two [11.8%] versus four [10.0%], P=1), bacteremia-related mortality (two [11.8%] versus one [2.5%], P=0.2), total mortality (five [33.3%] versus five [14.3%], P=1), or bacteremia relapse (three [17.7%] versus six [15.5%], P=1). There was no association between high level gentamicin-resistant strains and prior administration of antimicrobials within the preceding six weeks (12 [70.6%] for resistant strains versus 21 [53%] for susceptible strains, P=0.20) including aminoglycosides (two [11.8%] versus seven [17.5%], P=0.70), cephalosporins (seven [41.2%] versus 16 [40.4%], P=0.93), penicillins (eight [47.1%] versus 11 [27.5%], P=0.15), or vancomycin (four [23.5%] versus seven [17.5%], P=0.71).

Total mortality was similar in patients with *E faecalis* bacteremia due to high level gentamicin- or streptomycin-resistant strains and those with bacteremia due to high level gentamicin- or streptomycin-susceptible strains (nine of 35 and 10 of 33 for resistant strains versus 13 of 74 and 12 of 73 for susceptible strains, P=0.32 and 0.10, respectively). Attributable mortality, however, was significantly higher in patients with bacteremia due to high level streptomycin-resistant *E faecalis* strains compared with high level streptomycin-susceptible strains (four of 33 versus one of 73, P=0.03). It was similar in patients with bacteremia due to high level gentamicin-resistant *E faecalis* strains and high level gentamicin-susceptible strains (three of 35 versus two of 74, P=0.32). Patients with *E faecium* bacteremia due to ampicillin- or streptomycin-resistant strains and those with *E faecium* bacteremia due to susceptible strains had similar total mortality (four of seven and four of seven for resistant strains versus two of nine and two of eight for susceptible

strains, P=0.30 and 0.31, respectively) and attributable mortality (one of seven and one of seven for resistant strains versus zero of nine and zero of eight for susceptible strains, P=0.43 and 0.46, respectively). The mortality rate of patients with enterococcal isolates that were considered contaminants was also high (three of 11, 27.3%). In 82 (65.1%) episodes, patients completely recovered from their enterococcal bacteremia without any complications.

DISCUSSION

Enterococci accounted for 4% of all blood isolates at our institution. This proportion is relatively low compared with other reports where enterococci have been reported to cause 8.3% (26) and 11% (27) of episodes of bacteremia. Isolation of enterococci in blood cultures usually represented true pathogens, but in one-half of episodes, other pathogens were also present. *E faecalis* was the dominant species isolated in 85% of episodes, a finding consistent with other reports (20,28). However, several studies also report a predominance of *E faecium* (27,29) or a shift to *E faecium* with increasing resistance (30,31). Infections were usually hospital acquired after prolonged hospitalization, as other studies have consistently reported (20,21,29,30,32,33). The characteristics of infected patients, including old age, multiple underlying comorbidities, almost 90% with instrumentation and recent or current antimicrobial therapy, are also consistent with these previous reports. Intensive care units, medical and surgical wards, and hemodialysis units had the highest incidence of infection. Infection of central venous catheters was the most common source of enterococcal bacteremia, followed by urinary tract infections. Only 3% of the cases, all due to *E faecalis*, had endocarditis.

Complications of enterococcal bacteremia were uncommon, but included septic shock, persistent bacteremia for at least three days and relapse of bacteremia after appropriate antimicrobial therapy. Complications occurred as frequently when caused by an enterococcal species by itself or polymicrobial bacteremia. Of the 24 patients whose bacteremia was due to urinary tract infection, 25% had a relapse and 50% of relapses had associated bacteremia. The relapse rate of central venous catheter-associated enterococcal bacteremia treated with appropriate antimicrobial agents but without removal of the central catheter was 19%. Relapse of bacteremia did not occur in cases where central catheter infections were treated with removal of the catheter and antimicrobial therapy. Thus, this study suggests central catheter removal should be considered for enterococcal bacteremia.

The mortality of patients with enterococcal bacteremia was high, but this was mainly caused by underlying disease, consistent with previous studies. The observed overall mortality rate of 22% is lower than that in other reports (20,21,26, 28,29,30,33,34) where mortality rates of 30% to 63% and attributable mortality rates of 31% have been reported. However, it is consistent with one other report where mortality was 18% and attributable mortality was 8% (32). Factors associated with a higher attributable mortality included older age, presence of malignancy, infection with high level streptomycin-resistant *E faecalis* strains and lack of specific enterococcal antimicrobial therapy. In particular, attributable mortality was greater in subjects who did not receive empirical therapy that included enterococcal coverage.

All enterococcal isolates during the study were susceptible to vancomycin. Ampicillin resistance was identified only in *E faecium* isolates, whereas high level gentamicin resistance was identified only in *E faecalis* isolates. Both *E faecalis* and *E faecium* exhibited high level resistance to streptomycin. The only other Canadian report of enterococcal bacteremia also identified ampicillin resistance only in *E faecium* (30). In that study, 18% of all bacteremic isolates were high level gentamicin resistant versus none at our institution.

We did not observe any differences in patient characteristics or outcomes between those with high level gentamicin-susceptible or resistant strains, apart from a longer previous hospitalization in those with resistant strains. Other reports have described variable observations with respect to the presence or absence of aminoglycoside or ampicillin resistance and outcomes. Streptomycin and ampicillin resistance were linked, but exhibited by genetically different *E faecium* isolates. PFGE typing showed four strains among seven isolates, suggesting polyclonal origin.

CONCLUSIONS

These observations provide useful information that describes the epidemiology of enterococcal bacteremia at our institution before the arrival of VRE. They suggest that, at the time of this review, the extent and impact of enterococcal bacteremia at our institution was not as great as that reported from some other institutions. This study provides a baseline from which to monitor the evolution and impact of enterococcal bacteremia and resistance.

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