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Epidemiology and Antimicrobial Susceptibilities of Pathogens Isolated from Blood Cultures from Canadian Hospitals: CANWARD 2007-2013 Study

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ABSTRACT

Background: This study determined the epidemiology and antimicrobial susceptibilities of pathogens recovered from bloodstream infections (BSI) in Canadian hospitals (CH) from 2007-2013.
Methods: From 2007 through 2013, 14,874 pathogens from positive blood cultures were collected from 10 to15 tertiary-care centers across Canada. Susceptibility testing was performed using CLSI broth microdilution methods.
Results: 7340 (49.3%) Gram positives, 6790 (45.3%) Gram negatives and 734 (4.9%) yeasts were isolated. The 10 most common pathogens (representing 69.7% of all isolates; and excluding coagulase negative *Staphylococcus* species, 7.9%) were *Escherichia coli* (EC; 22.5%), *Staphylococcus aureus* [17.5%; including 13.6 % MSSA and 3.9% MRSA], *Klebsiella pneumoniae* (KP; 7.4%), *Streptococcus pneumoniae* (5.2%), *Enterococcus faecalis* (4.2%), *Pseudomonas aeruginosa* (3.9%), *Candida albicans* (2.9%), *Enterobacter cloacae* (2.3%), *Enterococcus faecium* (1.9%) and *Streptococcus agalactiae* (1.9%). Susceptibility rates (SR) for EC and KP were 100%, 99.6% meropenem (MER), 100%, 96.5% tigecycline (TGC), 99.8%, 99.0% ertapenem (ERT), 99.6%, 99.9% amikacin (AMK) 97.9%, 97.2% piperacillin-tazobactam (PTZ), 92.6%, 96.4% ceftriaxone (CTR), 90.0%, 97.4% gentamicin (GEN) and 78.0%, 93.6% ciprofloxacin (CIP), respectively. SR for *P. aeruginosa* were 97.6% AMK, 93.8% colistin, 90.3% ceftazidime, 89.1% PTZ, 88.4% GEN, 84.3% MER and 83.8% CIP. SR for MRSA were: 100% linezolid (LZD), 99.8% daptomycin (DAP), 99.8% TGC and 99.8% vancomycin (VAN). SR for *C. albicans* were 98.8% fluconazole, 99.1% voriconazole, 100% caspofungin, 100% micafungin, and 89.3% had an MIC of ≤ 1 for Amphotericin B. Between 2007 and 2013, the proportion of ESBL-producing EC and KP and VRE has at least doubled from 4.3-9.9%, 1.5-5.1%, 8.8% to 18.2% respectively. Of note, 4 carbapenemase-producing KP (CPKP) were identified (1 in 2009 and 3 in 2013). Patient demographics were as follows: 57.4/42.6% male/female, 10.9% ≤ 17 years, 45.4% 18-64 years and 43.7% ≥ 65 years.
Conclusions: The most active agents against Gram-negative bacilli were the carbapenems, AMK, and PTZ, while Gram-positive cocci, they were VAN, LZD and DAP. *C. albicans* remain highly susceptible to all agents tested. CPKP have emerged as a cause of BSI in CH.

BACKGROUND

Bloodstream infections cause significant morbidity and mortality and result in substantial health care costs. Recent studies in the United States and England indicate a high incidence of bloodstream infections (200,000 cases per year in the United States; 189,000 cases per year in England)(1,2). Reported mortality rates range between 18% and 60% based on a number of factors, including the causative agent (1,3). Empiric therapy is commonly administered early in the course of bloodstream infections (4). The epidemiology of bloodstream infections and antimicrobial susceptibility patterns of the causative agents vary over time (2,5). National surveillance studies that monitor the prevalence of pathogens and antimicrobial susceptibility profiles are essential to determine appropriate empiric treatment (6). This study assessed the epidemiology and antimicrobial resistance of pathogens associated with bloodstream infections in Canadian hospitals.

MATERIALS & METHODS

Study Design: From 2007 through 2013, 10-15 tertiary-care centres across Canada submitted pathogens from patients attending hospital clinics, emergency rooms, medical and surgical wards, and intensive care units.
Bacterial Strains: Stock cultures were stored at -80C in skim milk.
Antimicrobial Susceptibility Testing: Antimicrobial susceptibilities were determined via broth microdilution (CLSI).

RESULTS

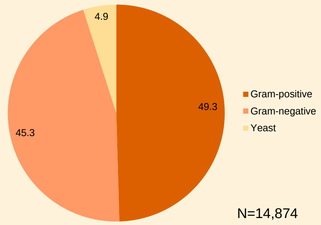

Figure 1. Distribution of pathogen groups recovered from bloodstream infections in Canadian hospitals from 2007-2013.

Table 1. The top ten most common pathogens causing bloodstream infections in Canadian hospitals.

Rank	Organism	% Total
1	*Escherichia coli*	22.5
2	*Staphylococcus aureus*	17.5 -13.6 MSSA & 3.9 MRSA
3	*Klebsiella pneumoniae*	7.4
4	*Streptococcus pneumoniae*	5.2
5	*Enterococcus faecalis*	4.2
6	*Pseudomonas aeruginosa*	3.9
7	*Candida albicans*	2.9
8	*Enterobacter cloacae*	2.3
9	*Enterococcus faecium*	1.9
10	*Streptococcus agalactiae*	1.9

Table 2. Demographics of the patients with bloodstream infections from CANWARD 2007-2013.

Demographics	%
Gender	
Female	42.6
Male	57.4
Age Group	
≤ 17 years	10.9
18-64 years	45.4
≥ 65 years	43.7
Location	
Hospital Clinic	7.5
Emergency Room	36.0
ICU	16.3
Medical	32.1
Surgical	8.0

Table 3 : Antimicrobial susceptibilities of the most common Gram-negative pathogens isolated from blood cultures from Canadian hospitals .

Organism /antimicrobial agent	%S	%I	%R	MIC50	MIC90	Range
***Escherichia coli* (n=3352)**						
Ceftriaxone	92.6	0.1	7.2	≤1	≤1	≤1 - >64
Ciprofloxacin	78.0	0.2	21.8	≤ 0.06	≤0.06	≤0.06 - >16
Gentamicin	90.0	0.3	9.7	≤0.5	8	≤0.5 - >32
Levofloxacin	78.5	0.4	21.1	≤0.06	16	≤0.06 - >32
Meropenem	100			≤0.12	≤0.12	≤0.12 – 0.5
Pip/Tazo	97.9	1.1	1.0	≤1	4	≤1 - >512
***Klebsiella pneumoniae* (n=1098)**						
Ceftriaxone	96.4	0.5	3.2	≤1	≤1	≤1 - >64
Ciprofloxacin	93.6	1.4	5.0	≤0.06	0.5	≤0.06 - >16
Gentamicin	97.4	03.4	2.2	≤0.5	≤0.5	≤0.5 - >32
Levofloxacin	95.6	1.5	2.8	≤0.06	0.5	≤0.06 - >32
Meropenem	99.6	0.2	0.2	≤0.12	≤0.12	≤0.12 - 8
Pip/Tazo	97.2	0.8	2.0	2	8	≤1 - >512
***Pseudomonas aeruginosa* (n=579)**						
Ceftazidime	90.3	2.6	7.2	4	8	1 - >32
Ciprofloxacin	83.8	3.8	12.4	0.25	8	≤0.06 - >16
Gentamicin	88.4	5.4	6.2	2	8	≤0.5 - >32
Levofloxacin	73.8	9.3	16.9	1	16	≤0.06 - >32
Meropenem	84.3	7.1	8.6	0.5	4	≤0.12 - >32
Pip/Tazo	89.1	5.9	5.0	4	32	≤1 - >512
***Enterobacter cloacae* (n=347)**						
Ceftriaxone	77.5	2.0	20.5	≤1	>64	≤1 - >64
Ciprofloxacin	93.4	1.7	4.9	≤0.06	0.25	≤0.06 - >16
Gentamicin	98.0	0.3	1.7	≤0.5	≤0.5	≤0.5 - >32
Levofloxacin	93.8	4.1	2.1	≤0.06	0.5	≤0.06 - 32
Meropenem	99.7	0.3		≤0.12	≤0.12	≤0.12 - 2
Pip/Tazo	87.9	6.3	5.8	2	32	≤1 - 256

Table 4 : Antifungal susceptibility against *C. albicans*, *C. glabrata* and *C. parapsilosis* isolated from blood cultures from Canadian hospitals.

Organism /antimicrobial agent	%S	%I /SDD [a]	%R	MIC50	MIC90	Range
***C. albicans* (n=428)**						
Amphotericin B				0.5	2	0.12 - 2
Caspofungin	94.6	5.4		0.12	0.25	≤0.015 – 0.5
Fluconazole	98.4	0.7	0.9	0.12	0.5	≤0.0.6 - >64
Flucytosine				0.12	1	≤0.03 - >64
Itraconazole				≤0.12	≤0.12	≤0.12 – 0.5
Ketoconazole				≤1	4	≤1 - >512
Micafungin	100			≤0.015	≤0.015	≤0.015–0.25
Posaconazole[b]	97.7			≤0.015	0.06	≤0.015 - >16
Voriconazole	99.1	0.2	0.7	≤0.015	0.03	≤0.015 - >16
***C. glabrata* (n=144)**						
Amphotericin B				1	2	0.12 – 2
Caspofungin	77.8	19.4	2.8	0.25	0.5	0.03 - 2
Fluconazole	97.3	0.9	1.8	4	16	≤0.06 – 128
Flucytosine				≤0.03	0.06	≤0.03 - 2
Itraconazole				0.5	1	0.03 - >16
Ketoconazole				0.25	1	0.03 - 4
Micafungin	97.4	1.3	1.3	≤0.015	≤0.015	≤0.015–0.25
Posaconazole				0.25	1	≤0.015-2
Voriconazole				0.12	1	0.015 - 4
***C. parapsilosis* (n=75)**						
Amphotericin B				1	2	0.25 - 2
Caspofungin	92.3	7.7		1	2	0.06 - 4
Fluconazole	95.9	4.1		0.5	2	≤0.06 - 32
Flucytosine				0.12	0.12	≤0.03 – 0.25
Itraconazole				0.06	0.25	≤0.015 – 2
Ketoconazole				0.03	0.06	0.015 – 1
Posaconazole[b]	96.7			≤0.015	0.06	≤0.015–0.12
Voriconazole	93.9	2.0	4.1	0.015	0.06	≤0.015 - 1

[a] SDD: Susceptible Does Dependent: Fluconazole and Voriconazole, [b] EUCAST Breakpoint: S=0.06 µg/mL

Table 5 : Antimicrobial susceptibilities of the most common Gram-positive pathogens isolated from blood cultures from Canadian hospitals .

Organism /antimicrobial agent	%S	%I	%R	MIC_{50}	MIC_{90}	Range
MSSA (n=2018)						
Ceftriaxone				4	4	≤1 - 256
Daptomycin	100			0.25	0.25	≤0.06 – 1
Levofloxacin	89.9	0.2	9.9	0.25	2	≤0.06 - >32
Linezolid	100			2	2	≤0.12 – 4
Meropenem				0.12	0.25	≤0.12 – 4
Pip/Tazo				≤1	≤1	≤1 - 32
Vancomycin	100			1	1	≤0.25 - 2
MRSA (n=575)						
Ceftriaxone			100	>64	>64	2 - >64
Daptomycin	99.8		0.2	0.25	0.25	0.06 - 2
Levofloxacin	13.5		86.5	>32	>32	0.12 - >32
Linezolid	100			2	2	0.25 – 4
Meropenem				8	32	0.12 - >32
Pip/Tazo				64	128	2 – 256
Vancomycin	99.8	0.2		1	1	≤0.25 - 4
CNS (n=695)						
Ceftriaxone				>4	>4	≤1 - >4
Daptomycin	100			0.12	0.25	≤0.06 – 0.5
Levofloxacin	45.2	1.6	53.2	4	>32	0.12 - >32
Linezolid	100			0.5	1	≤0.12 – 4
Meropenem				2	32	≤0.12 - >32
Pip/Tazo				≤1	32	≤1 - 128
Vancomycin	100			1	2	≤0.25 - 2
***Streptococcus pneumoniae* (n=738)**						
Ceftriaxone	99.7	0.3		≤0.12	≤0.12	≤0.12 – 2
Daptomycin				0.06	0.12	0.06 – 0.12
Levofloxacin	99.3	0.1	0.5	0.5	1	≤0.06 - 16
Linezolid	100			1	1	≤0.12 - 2
Meropenem	97.8	1.0	1.2	≤0.06	≤0.06	≤0.06 – 1
Pip/Tazo				≤1	≤1	≤1 – 8
Vancomycin	100			≤0.25	0.25	≤0.25 - 1
***Enterococcus faecalis* (n=624)**						
Ceftriaxone				>64	>64	≤0.25 - >64
Daptomycin	100			0.5	1	≤0.06 – 4
Levofloxacin	63.7	1.1	35.2	2	>32	0.25 - >32
Linezolid	97.6	2.4		2	2	0.5 – 4
Meropenem				4	8	≤0.06 - >32
Pip/Tazo				4	8	≤1 – 512
Vancomycin	100			1	2	0.25 – 4
***Enterococcus faecium* (n=286)**						
Ceftriaxone				>64	>64	0.5 - >64
Daptomycin	100			1	2	≤0.03 – 4
Levofloxacin	10.6	1.5	87.9	>32	>32	1 - >32
Linezolid	90.6	9.4		2	≤0.12	2 - 4
Meropenem				>32	>32	2 - >32
Pip/Tazo				>512	>512	2 - >512
Vancomycin	80.8		19.2	1	>32	≤0.25 - >32

S: Susceptible; I: Intermediate, R: Resistant, MSSA: Methicillin Susceptible *Staphylococcus aureus*, MRSA: Methicillin Resistant *Staphylococcus aureus*, CNS: coagulase-negative staphylococci, Pip/Tazo: Piperacillin-Tazobactam, [a] SDD: Susceptible Does Dependent: Fluconazole and Voriconazole, [b] EUCAST Breakpoint: S=1 µg/mL, [c] EUCAST Breakpoint: S=0.06 µg/mL

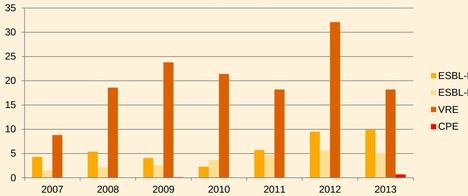

Figure 2. Proportion of antimicrobial resistant organisms isolated from blood cultures.

ESBL: Extended-spectrum β-lactamase, EC: *E. coli*, KP: *K. pneumoniae*, VRE: vancomycin resistant enterococci, CPE: carbapenemase-producing *Enterobacteriaceae*

CONCLUSIONS

1. From 2007 through 2013, 14,874 pathogens from positive blood cultures were collected from 10-15 tertiary care centers across Canada.
2. Of the 14,874, 7340 (49.3%) Gram-positives, 6790 (45.3%) Gram-negatives and 734 (4.9%) yeasts were isolated.
3. The most common Gram-positive pathogens were *S. aureus*, *S. pneumoniae, E. faecalis*, *E. faecium* and *S. agalactiae.*
4. The most common Gram-negative pathogens were *E. coli*, *K. pneumoniae*, *P. aeruginosa* and *E. cloacae*.
5. *C. albicans* was the seventh most commonly isolated organism from blood cultures and remains highly susceptible to all antifungal agents tested in this study.
6. The proportion of ESBL-producing *E. coli* and *K. pneumoniae* and VRE has at least doubled from 4.3-9.9%, 1.5-8.8% and 8.8-18.2%, respectively.
7. The most active agents against Gram positive cocci were vancomycin, linezolid and daptomycin.
8. The most active agents against Gram-negative bacilli were the carbapenems, amikacin and piperacillin-tazobactam.

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