

Antimicrobial Susceptibility of 49,319 Pathogens Isolated from Patients in Canadian Hospitals:

12 Years of the CANWARD Study 2007-2018

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Introduction

Antimicrobial resistant Gram-positive organisms such as methicillin-resistant *Staphylococcus aureus* (MRSA, community associated [CA] and healthcare associated [HA]), vancomycin-resistant *Enterococcus species* (VRE), penicillin-resistant *Streptococcus pneumoniae*, and Gram-negative bacilli such as extended spectrum β -lactamase (ESBL) producing *Escherichia coli* and *Klebsiella* species as well as fluoroquinolone-resistant and carbapenem-resistant Enterobacteriaceae and *Pseudomonas aeruginosa* are increasing in prevalence in Canada and around the world (1, 2). Available therapeutic options for the treatment of these antibiotic resistant organisms are limited as these organisms frequently display a multidrug resistant (MDR) and potentially an extremely drug resistant (XDR) phenotype (1, 2).

CANWARD (a collaboration between the Canadian Antimicrobial Resistance Alliance and the National Microbiology Laboratory) is a national ongoing surveillance study which assess pathogens associated with and antimicrobial resistance patterns in respiratory, bacteremic, urinary, and wound/IV site infections in Canadian hospitalized patients on medical/surgical wards, intensive care units, emergency rooms and outpatient clinics.

Materials and Methods

Participating Sites

From January 2007 to October 2018, tertiary-care medical centres in major population centres in 8 of the 10 provinces in Canada were recruited (1, 2). These sites were geographically distributed in a population based fashion.

Bacterial Isolates

Tertiary-care medical centres submitted pathogens from patients attending hospital clinics, emergency rooms, medical and surgical wards, and intensive care units. Each study site was asked to submit clinical isolates (consecutive, one per patient, per infection site) from inpatients and outpatients with respiratory, urine, wound, and bloodstream infections. Isolate identification was performed by the submitting site and confirmed at the reference site as required, based on morphological characteristics and antimicrobial susceptibility patterns. Isolates were shipped on Amies semi-solid transport media to the coordinating laboratory (Health Sciences Centre, Winnipeg, Canada), subcultured onto appropriate media, and stocked in skim milk at -80°C until minimum inhibitory concentration (MIC) testing was carried out. From 2007-2018, 7718, 5283, 5373, 4960, 3785, 2802, 3511, 3172, 3206, 3126, 3420 and 2963 isolates were collected in each study year (1, 2).

Antimicrobial Susceptibilities

The *in vitro* activity of selected antimicrobials was determined by broth microdilution in accordance with (CLSI) guidelines (3). Antimicrobial minimum inhibitory concentration (MIC) interpretive standards were defined according to CLSI breakpoints (4). The MICs of the antimicrobial agents were determined using 96-well custom designed microtitre plates. These plates contained doubling antimicrobial dilutions in 100 μ L/well of cation adjusted Mueller-Hinton broth and inoculated to achieve a final concentration of approximately 5 x 10⁵ CFU/mL then incubated in ambient air for 24 hours prior to reading. Colony counts were performed periodically to confirm inocula. Quality control was performed using ATCC QC organisms including *S. pneumoniae* 49619, *S. aureus* 29213, *E. faecalis* 29212, *E. coli* 25922, and *P. aeruginosa* 27853.

Results

Table 1. Antimicrobial activity against the most common Gram-positive cocci isolated from Canadian hospitals

Organism (no. tested) / Antimicrobial Agent	% S	% I	% R	MIC (μ g/mL)				
				MIC ₅₀	MIC ₉₀	Range Min	Range Max	Range
Staphylococcus aureus, MSSA (8243)								
Cefoxitin	99.6	0.4	4	4	0.12	> 32		
Ceftazidime	100.0			≤ 1	≤ 1	≤ 1	2	
Ceftriaxone				4	4	≤ 0.25	256	
Ciprofloxacin	86.5	3.1	10.4	0.5	4	≤ 0.06	> 16	
Clarithromycin	75.7	0.6	23.7	0.25	> 32	≤ 0.03	> 32	
Daptomycin	93.6	0.4	5.9	≤ 0.25	≤ 0.25	≤ 0.25	> 8	
Doxycycline	99.99	0.01	0.25	0.5	≤ 0.03	2		
Gentamicin	98.9	0.8	0.4	≤ 0.12	0.25	≤ 0.12	32	
Levofloxacin	98.14	0.09	1.77	≤ 0.5	≤ 0.5	≤ 0.5	> 32	
Linezolid	99.99	0.01	2	4	≤ 0.12	> 16		
Moxifloxacin	90.6	0.8	8.6	≤ 0.06	0.25	≤ 0.06	> 16	
Nitrofurantoin	99.88	0.03	0.09	16	16	≤ 0.5	256	
Telavancin	100.0			0.06	0.06	0.008	0.12	
Tigecycline	99.8	0.2	0.12	0.25	0.03	2		
Tobramycin	97.3	0.3	2.5	≤ 0.5	≤ 0.5	≤ 0.5	> 64	
Trimethoprim Sulfamethoxazole	99.5	0.5	≤ 0.12	≤ 0.12	≤ 0.12	> 8		
Vancomycin	100.0			1	1	≤ 0.12	2	
Staphylococcus aureus, MRSA (2214)								
Cefoxitin	0.2	99.8	> 32	> 32	1	> 32		
Ceftazidime	100.0			≤ 1	≤ 1	≤ 1	4	
Ceftriaxone				> 64	> 64	2	> 256	
Ciprofloxacin	18.5	0.3	81.2	> 16	> 16	≤ 0.06	> 16	
Clarithromycin	16.0	0.4	83.6	> 32	> 32	0.03	> 32	
Daptomycin	56.0	0.0	44.0	≤ 0.12	> 8	≤ 0.12	> 8	
Doxycycline	99.9	0.1	0.25	0.5	0.06	4		
Gentamicin	97.7	0.9	1.4	≤ 0.12	1	≤ 0.12	16	
Levofloxacin	93.2	0.3	6.5	0.5	1	≤ 0.5	> 32	
Linezolid	100.0			83.5	> 32	> 32	> 12	> 32
Moxifloxacin	100.0			2	4	≤ 0.12	4	
Nitrofurantoin	19.0	3.8	77.2	8	> 16	≤ 0.06	> 16	
Telavancin	99.8	0.1	0.1	16	16	128	8	
Tigecycline	100.0			0.06	0.06	0.008	0.12	
Tobramycin	98.8	1.2	2.25	0.5	0.03	2		
Trimethoprim Sulfamethoxazole	94.4	6.1	37.7	≤ 0.5	> 64	≤ 0.5	> 64	
Vancomycin	99.9	0.1	5.6	≤ 0.12	≤ 0.12	> 8		
Streptococcus epidermidis (10599)								
Amox-Clav				1	8	≤ 0.06	32	
Cefazolin				1	32	≤ 0.5	> 128	
Cefepime				4	64	≤ 0.25	128	
Ceftriaxone				8	> 32	≤ 0.06	> 32	
Ceftazidime				≤ 1	≤ 1	≤ 1	4	
Ciprofloxacin	46.0	1.5	52.6	4	> 16	≤ 0.06	> 16	
Clarithromycin	33.7	1.4	64.9	> 32	> 32	≤ 0.03	> 32	
Daptomycin	58.1	1.5	40.4	≤ 0.12	> 8	≤ 0.12	> 8	
Doxycycline	99.9	0.1	0.25	0.25	≤ 0.03	2		
Gentamicin	96.0	1.8	2.2	0.25	1	≤ 0.12	32	
Levofloxacin	58.7	6.1	35.2	≤ 0.5	> 32	≤ 0.5	> 32	
Linezolid	47.3	1.1	51.6	4	> 32	0.12	> 32	
Moxifloxacin	100.0			0.5	1	≤ 0.12	4	
Nitrofurantoin	47.8	8.9	43.3	1	> 16	≤ 0.06	> 16	
Pip-Tazo				≤ 1	16	≤ 1	128	
Telavancin				0.06	0.12	0.004	0.5	
Tigecycline	99.3	0.7	0.12	0.5	≤ 0.03	1		
Tobramycin				≤ 0.5	32	≤ 0.5	> 64	
Trimethoprim Sulfamethoxazole	60.9	39.1	1	8	≤ 0.12	> 8		
Vancomycin	100.0			1	2	≤ 0.25	4	
Streptococcus pneumoniae (2868)								
Amox-Clav	97.8	1.4	0.8	≤ 0.06	0.12	≤ 0.06	16	
Ceftazidime	99.9			≤ 0.06	≤ 0.06	≤ 0.06	4	
Ceftriaxone	99.5	0.4	0.1	≤ 0.12	≤ 0.12	≤ 0.06	1	
Cefuroxime	93.2	1.9	4.9	≤ 0.25	≤ 0.25	≤ 0.25	> 16	
Chloramphenicol	98.0	2.0	2	4	≤ 0.12	32		
Ciprofloxacin	97.1	2.9	1	2	≤ 0.06	> 16		
Clarithromycin	78.5	3.3	18.1	≤ 0.03	4	≤ 0.03	> 32	
Daptomycin	92.6	0.5	6.8	≤ 0.12	≤ 0.12	≤ 0.12	> 64	
Doxycycline	86.6	1.2	12.2	≤ 0.25	2	≤ 0.25	> 16	
Ertapenem	99.0	1.0	0.0	≤ 0.06	0.12	≤ 0.06	4	
Impipenem	93.4	4.7	1.9	≤ 0.03	≤ 0.03	≤ 0.03	1	
Levofloxacin	99.0	0.2	0.8	1	1	≤ 0.06	16	
Linezolid	100.0			0	1	≤ 0.12	4	
Meropenem	95.2	3.1	1.7	≤ 0.06	≤ 0.06	≤ 0.06	2	
Moxifloxacin	99.1	0.4	0.4	0.12	0.25	≤ 0.06	8	
Penicillin	82.6	13.0	4.4	≤ 0.03	0.25	≤ 0.03	> 8	
Pip-Tazo				≤ 1	≤ 1	≤ 1	8	
Telavancin				0.015	0.015	≤ 0.002	0.06	
Tigecycline	99.7	0.3	0.03	0.06	≤ 0.015	0.25		
Trimethoprim Sulfamethoxazole	85.2	6.1	8.7	≤ 0.12	2	≤ 0.12	> 8	
Vancomycin	100.0			≤ 0.25	≤ 0.25	≤ 0.25	1	
Streptococcus agalactiae (792)								
Amox-Clav				≤ 0.06	≤ 0.06	≤ 0.06	0.25	
Ceftazidime				≤ 0.06	≤ 0.06	≤ 0.06	≤ 0.06	
Ceftriaxone	100.0			≤ 0.12	≤ 0.12	≤ 0.06	0.5	
Cefuroxime				≤ 0.25	≤ 0.25	≤ 0.25	0.5	
Chloramphenicol	96.8	2.9	0.2	4	4	0.5	16	
Ciprofloxacin				0.5	1	0.25	> 16	
Clarithromycin	66.1	3.6	30.3	≤ 0.03	> 32	≤ 0.03	> 32	
Daptomycin	81.1	0.8	18.1	≤ 0.12	> 64	≤ 0.12	> 64	
Doxycycline	100.0			0.25	0.25	≤ 0.03	1	
Ertapenem				8	16	≤ 0.25	> 16	
Impipenem				≤ 0.06	≤ 0.06	≤ 0.06	0.12	
Levofloxacin	96.3	3.7	0.5	1	0.25	> 32		
Linezolid	97.4	2.6	1	2	≤ 0.12	4		
Meropenem	100.0			≤ 0.06	≤ 0.06	≤ 0.06	0.12	
Moxifloxacin				0.12	0.25	≤ 0.06	16	
Penicillin	99.8	0.2	0.06	0.12	0.03	0.25		
Pip-Tazo				≤ 1	≤ 1	≤ 1	≤ 1	
Telavancin	100.0			0.06	0.06	0.015	0.12	
Tigecycline	99.8	0.2	0.06	0.12	≤ 0.015	1		
Trimethoprim Sulfamethoxazole				≤ 0.12	≤ 0.12	≤ 0.12	1	
Vancomycin	100.0			0.5	0.5	≤ 0.25	1	
Streptococcus pyogenes (724)								
Amox-Clav				≤ 0.06	≤ 0.06	≤ 0.06	1	
Ceftazidime				≤ 0.06	≤ 0.06	≤ 0.06	0.5	
Ceftriaxone	100.0			≤ 0.12	≤ 0.12	≤ 0.06	0.25	
Cefuroxime				≤ 0.25	≤ 0.25	≤ 0.25	1	
Chloramphenicol	97.1	2.6	0.3	2	4	0.5	32	
Ciprofloxacin				0.5	1	≤ 0.06	> 16	
Clarithromycin	89.4	1.9	8.7	≤ 0.03	0.5	≤ 0.03	> 32	
Daptomycin	98.0			2.0	≤ 0.12	≤ 0.12	> 64	
Doxycycline	100.0			0.06	0.12	≤ 0.03	0.25	
Ertapenem				≤ 0.25	0.5	≤ 0.25	> 16	
Impipenem				≤ 0.06	≤ 0.06	≤ 0.06	1	
Levofloxacin	99.8	0.2	0.5	1	0.06	16		
Linezolid	99.3	0.7	1	2	≤ 0.12	4		
Meropenem	100.0			≤ 0.06	≤ 0.06	≤ 0.06	0.25	
Moxifloxacin				0.12	0.25	≤ 0.06	4	
Penicillin	100.0			≤ 0.03	≤ 0.03	≤ 0.03	0.12	
Pip-Tazo				≤ 1	≤ 1	≤ 1	4	
Telavancin	100.0			0.03	0.06	0.015	0.06	
Tigecycline	100.0			0.03	0.06	≤ 0.015	0.25	
Trimethoprim Sulfamethoxazole				≤ 0.12	≤ 0.12	≤ 0.12	> 8	
Vancomycin	100.0			0.5	0.5	≤ 0.12	1	
Enterococcus faecalis (1424)								
Amox-Clav				0.5	1	≤ 0.06	32	
Ceftazidime				≤ 1	≤ 1	≤ 1	> 16	
Ceftriaxone	62.5	10.8	26.7	1	> 16	≤ 0.06	> 16	
Ciprofloxacin				2	> 32	≤ 0.03	> 32	
Daptomycin	88.8	11.2	0.5	2	≤ 0.03	4		
Doxycycline				4	4	0.12	16	
Ertapenem	36.6	41.3	22.1	8	16	≤ 0.12	32	
Impipenem				16	16	0.25	> 32	
Levofloxacin	63.9	1.8	34.4	2	> 32	0.5	> 32	
Linezolid	91.4	8.6	2	2	2	0.5	4	
Meropenem				4	8	≤ 0.06	> 32	
Moxifloxacin				0.25	16	≤ 0.06	> 16	
Nitrofurantoin	99.5	0.5	8	16	≤ 0.5	64		
Pip-Tazo				4	4	≤ 1	> 512	
Tigecycline	98.1	1.9	0.12	0.25	≤ 0.03	1		
Tobramycin				16	> 64	≤ 0.5	> 64	
Vancomycin	100.0			1	2	0.25	4	
Enterococcus faecium (572)								
Amox-Clav				> 32	> 32	≤ 0.06	> 32	
Ceftazidime				> 16	> 16	≤ 1	> 16	
Ciprofloxacin	6.9	1.6	91.5	> 16	> 16	0.25	> 16	
Clarithromycin				> 32	> 32	≤ 0.03	> 32	
Daptomycin	58.9	40.9	0.2	1	2	0.03	8</	