

Antimicrobial Susceptibility of 46,356 Pathogens Isolated from Patients in Canadian Hospitals:

11 Years of the CANWARD Study 2007-2017

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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 B-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 2017, 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 2007-2017, 7718, 5283, 5373, 4960, 3785, 2802, 3511, 3172, 3206, 3126 and 3420 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 100µL/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 (µg/mL)			
				MIC ₅₀	MIC ₉₀	Range	Range Max
Staphylococcus aureus, MSSA (7753)							
Cefoxitin	99.60	0.40	4	4	0.12	32	
Ceftobiprole ^a	100.00			≤1	≤1	≤1	2
Ceftriaxone				4	4	≤1	> 64
Ciprofloxacin	86.43	3.07	10.49	0.5	4	≤0.06	> 16
Clarithromycin	75.69	0.61	23.70	0.25	32	≤0.03	> 32
Clindamycin	93.56	0.40	6.04	≤0.25	≤0.25	≤0.25	> 8
Daptomycin	100.00			0.25	0.25	≤0.03	1
Doxycycline	98.86	0.83	0.31	≤0.12	0.25	≤0.12	32
Gentamicin	98.13	0.08	1.80	≤0.5	≤0.5	≤0.5	> 32
Levofloxacin	90.10	0.33	9.57	0.25	1	≤0.06	> 32
Linezolid	100.00			2	4	≤0.12	4
Moxifloxacin	90.54	0.75	8.71	≤0.06	0.25	≤0.06	> 16
Nitrofurantoin	99.93	0.03	0.03	16	16	≤0.5	256
Telavancin	100.00			0.06	0.06	0.008	0.12
Tigecycline ^b	99.84	0.16	0.12	0.25	0.03	2	2
Tobramycin	97.22	0.28	2.49	≤0.5	≤0.5	≤0.5	> 64
Trimethoprim Sulfam	99.51	0.49	≤0.12	≤0.12	≤0.12	> 8	> 8
Vancomycin	100.00			1	1	≤0.25	2
Staphylococcus aureus, MRSA (2078)							
Cefoxitin	0.16	99.84	> 32	> 32	1	> 32	
Ceftobiprole	99.73	0.27	≤1	2	≤1	4	
Ceftriaxone			> 64	> 64	2	> 256	
Ciprofloxacin	18.19	0.34	81.47	> 16	> 16	≤0.06	> 16
Clarithromycin	15.50	0.39	84.11	> 32	> 32	≤0.03	> 32
Clindamycin	55.09	0.05	44.86	≤0.25	> 8	≤0.25	> 8
Daptomycin	99.90	0.10	0.25	0.5	0.06	4	
Doxycycline	97.72	1.04	1.24	≤0.12	1	≤0.12	16
Gentamicin	93.17	0.29	6.54	≤0.5	1	≤0.5	> 32
Levofloxacin	14.06	85.94	> 32	> 32	12	> 32	
Linezolid	100.00			2	4	≤0.12	4
Moxifloxacin	18.67	3.66	77.67	8	> 16	≤0.06	> 16
Nitrofurantoin	99.87	0.13	16	16	8	64	
Telavancin	100.00			0.06	0.06	0.008	0.12
Tigecycline	99.13	0.87	0.25	0.5	≤0.03	2	2
Tobramycin	60.14	0.93	38.92	≤0.5	> 64	≤0.5	> 64
Trimethoprim Sulfam	94.32	5.68	≤0.12	≤0.12	≤0.12	> 8	> 8
Vancomycin	99.86	0.14	1	1	≤0.25	4	
Staphylococcus epidermidis (1022)							
Amoxicillin Clavulanate			1	8	≤0.06	32	
Cefazolin			1	64	≤0.5	> 128	
Cefepime			4	64	≤0.25	128	
Cefoxitin			8	> 32	≤0.06	> 32	
Ceftobiprole			≤1	≤1	≤1	4	
Ceftriaxone			8	> 64	≤0.25	> 256	
Ciprofloxacin	46.25	1.38	52.37	4	> 16	≤0.06	> 16
Clarithromycin	33.27	1.48	65.25	> 32	> 32	≤0.03	> 32
Clindamycin	58.14	1.38	40.47	≤0.25	> 8	≤0.25	> 8
Daptomycin	100.00			0.12	0.25	≤0.03	1
Doxycycline	96.55	1.54	1.92	0.25	1	≤0.12	32
Gentamicin	57.76	5.84	36.40	≤0.5	> 32	≤0.5	> 32
Levofloxacin	44.24	1.56	54.21	4	> 32	12	> 32
Linezolid	100.00			0.5	1	≤0.12	4
Moxifloxacin	47.93	8.78	43.29	1	> 16	≤0.06	> 16
Pip-Tazo				≤1	16	≤1	128
Telavancin	99.19	0.81	0.06	0.12	0.004	0.25	2
Tigecycline	99.31	0.69	0.12	0.25	≤0.03	1	1
Tobramycin	63.51	12.55	23.94	≤0.5	32	≤0.5	> 64
Trimethoprim Sulfam	60.55	39.45	1	8	≤0.12	> 8	> 8
Vancomycin	100.00			1	2	≤0.25	4
Streptococcus pneumoniae (2743)							
Amoxicillin Clavulanate	97.90	1.22	0.88	≤0.06	0.12	≤0.06	16
Ceftobiprole	99.89	0.11	≤0.06	≤0.06	≤0.06	1	1
Ceftriaxone	99.43	0.42	0.15	≤0.12	≤0.12	≤0.12	4
Cefuroxime	93.34	1.87	4.78	≤0.25	≤0.25	≤0.25	> 16
Chloramphenicol	98.72	1.28	2	4	≤0.12	32	
Ciprofloxacin	97.01	2.99	1	2	≤0.06	> 16	
Clarithromycin	78.51	3.45	18.04	≤0.03	4	≤0.03	> 32
Clindamycin	92.72	0.54	6.74	≤0.12	≤0.12	> 64	> 64
Daptomycin				≤0.06	≤0.06	≤0.06	0.5
Doxycycline	86.82	1.23	11.95	≤0.25	2	≤0.25	> 16
Ertapenem	99.00	0.96	0.04	≤0.06	0.12	≤0.06	4
Impipenem	93.51	4.62	1.87	≤0.03	≤0.03	≤0.03	4
Levofloxacin	99.08	0.15	0.77	1	1	≤0.06	32
Linezolid	99.96	0.04	1	1	1	≤0.12	4
Meropenem	95.37	2.99	1.65	≤0.06	≤0.06	≤0.06	2
Moxifloxacin	99.12	0.42	0.46	0.12	0.25	≤0.06	8
Penicillin	82.63	13.07	4.30	≤0.03	0.25	≤0.03	> 8
Pip-Tazo				≤1	≤1	≤1	8
Telavancin				0.015	0.015	≤0.002	0.03
Tigecycline	99.73	0.27	0.03	0.06	≤0.015	0.25	2
Trimethoprim Sulfam	84.98	6.21	8.81	≤0.12	2	≤0.12	> 8
Vancomycin	100.00			≤0.25	≤0.25	≤0.25	1

^a For tigecycline, FDA approved breakpoints applied.
^b For ceftobiprole, EUCAST breakpoints applied. Not all isolates tested with ceftobiprole.

Organism (no. tested) / Antimicrobial Agent	% S	% I	% R	MIC (µg/mL)			
				MIC ₅₀	MIC ₉₀	Range	Range Max
Streptococcus agalactiae (742)							
Amoxicillin Clavulanate				≤0.06	≤0.06	≤0.06	0.25
Ceftobiprole				≤0.06	≤0.06	≤0.06	≤0.06
Ceftriaxone	100.00			≤0.12	≤0.12	≤0.12	0.5
Cefuroxime				≤0.25	≤0.25	≤0.25	0.5
Chloramphenicol	97.50	2.22	0.28	4	4	0.5	16
Ciprofloxacin				0.5	1	0.25	> 16
Clarithromycin	66.74	4.02	29.24	≤0.03	32	≤0.03	> 32
Clindamycin	82.14	0.67	17.19	≤0.12	> 64	≤0.12	> 64
Daptomycin	100.00			0.25	0.25	≤0.03	0.5
Doxycycline				8	16	≤0.25	> 16
Ertapenem	100.00			≤0.06	≤0.06	≤0.06	0.12
Impipenem				≤0.03	0.03	≤0.03	0.12
Levofloxacin	96.21	3.79	1	1	0.25	> 32	> 32
Linezolid	97.32	2.68	1	2	≤0.12	4	
Meropenem	100.00			≤0.06	≤0.06	≤0.06	0.12
Moxifloxacin				0.12	0.25	≤0.06	16
Nitrofurantoin	99.78	0.22	0.06	0.12	0.03	0.25	0.25
Penicillin				≤0.1	0.1	≤1	≤1
Pip-Tazo				≤0.6	0.6	0.15	0.06
Telavancin	100.00			0.06	0.06	0.015	1
Tigecycline	99.78	0.22	0.06	0.06	≤0.015	1	1
Trimethoprim Sulfam				≤0.12	≤0.12	≤0.12	1
Vancomycin	100.00			0.5	0.5	≤0.25	1
Streptococcus pyogenes (690)							
Amoxicillin Clavulanate				≤0.06	≤0.06	≤0.06	1
Ceftobiprole				≤0.06	≤0.06	≤0.06	0.5
Ceftriaxone	99.85	0.15	≤0.12	≤0.12	≤0.12	1	1
Cefuroxime				≤0.25	≤0.25	≤0.25	1
Chloramphenicol	98.39	1.29	0.32	2	4	0.5	32
Ciprofloxacin				0.5	1	≤0.06	> 16
Clarithromycin	89.33	1.98	8.69	≤0.03	0.5	≤0.03	> 32
Clindamycin	98.02	1.98	≤0.12	≤0.12	≤0.12	> 64	> 64
Daptomycin	100.00			0.06	0.12	≤0.03	0.25
Doxycycline				≤0.25	0.5	≤0.25	> 16
Ertapenem	100.00			≤0.06	≤0.06	0.1	1
Impipenem				≤0.03	0.03	≤0.03	0.25
Levofloxacin	99.70	0.15	0.15	0.5	1	≤0.06	16
Linezolid	99.39	0.61	1	2	≤0.12	4	
Meropenem	100.00			≤0.06	≤0.06	≤0.06	0.25
Moxifloxacin				0.12	0.25	≤0.06	4
Nitrofurantoin	100.00			≤0.03	0.03	≤0.03	0.12
Penicillin				≤0.03	0.03	≤0.03	0.12
Pip-Tazo				≤1			