

Antimicrobial Susceptibility of 36,607 Pathogens Isolated from Patients in Canadian Hospitals: CANWARD Study 2007-2014

G.G. ZHANEL¹, H.J. ADAM^{1,2}, M. BAXTER¹, B. WESHNOWSKI², R. VASHISHT¹, M. ISMATH¹, R. HINK¹, K. NICHOL², A. DENISUIK¹, A. GOLDEN¹, P. LAGACÉ-WIENS^{1,2}, J.A. KARLOWSKY^{1,2}, M. GILMOUR^{1,3}, D. BAY¹, M.R. MULVEY^{1,3}, and the CANADIAN ANTIMICROBIAL RESISTANCE ALLIANCE (CARA)

¹University of Manitoba, ²Diagnostic Services Manitoba, and the ³National Microbiology Laboratory, Winnipeg, Manitoba, Canada

ABSTRACT

Background: CANWARD is a national, annual Health Canada endorsed surveillance study assessing pathogens causing infections in Canadian hospitals and their antimicrobial resistance patterns.

Methods: From 2007 to 2014, 36,607 pathogens were collected from tertiary-care hospitals across Canada. Antimicrobial susceptibility testing was performed using CLSI broth microdilution methods with >45 marketed and investigational agents.

Results: Specimen source composition of the 36,607 isolates was 44.1% blood, 32.0% respiratory, 13.7% urine and 10.2% wound specimens. Patient demographic characteristics were: 54.6/45.4% male/female; 13.0/44.6/42.4% patients aged ≤17/18-64/≥65 years; and 37.8/25.2/19.1/18.0% patients located in medical and surgical wards/emergency rooms/ICUs/clinics. The most common pathogens were: *E. coli* (EC 19.7%), MSSA (16.4%), *P. aeruginosa* (PA 8.7%), *S. pneumoniae* (SPN 6.5%), *K. pneumoniae* (KP 6.1%), MRSA (4.7%), *Enterococcus* spp. (4.0%), and *H. influenzae* (4.0%). Susceptibility rates (SR) for EC were: 99.9% for meropenem (MER) and tigecycline (TGC), 99.7% ertapenem (ERT), 97.7% piperacillin-tazobactam (PTZ), 92.5% ceftriaxone (CTR), 90.4% gentamicin (GEN), 77.2% ciprofloxacin (CIP) and 73.0% TMP-SMX (SXT). SR for PA were: 94.2% colistin, 84.3% PTZ, 83.3% ceftazidime (CAZ), 81.2% MER, 77.6% GEN and 74.1% CIP. SR for MRSA were: 100% for linezolid (LZD) and telavancin (TLV), 99.9% daptomycin (DAP), 99.4% TGC, 99.1% vancomycin, and 93.3% SXT. Rates of resistant organisms between 2007-2014 increased significantly for ESBL-producing EC (3.4%-11.6%) and KP (1.5%-6.5%) as well as VRE (1.8%-7.0%), whereas MRSA rates (26.1%-20.2%) significantly declined.

Conclusions: EC, MSSA, PA, SPN, KP, and MRSA are the most common pathogens in Canadian hospitals. SR for EC were highest for MER, TGC, ERT and PTZ. SR for PA were highest for colistin, PTZ, CAZ and MER. 99-100% of MRSA were susceptible DAP, LZD, TLV, and vancomycin.

MATERIALS & METHODS

Participating Sites:

From January 2007 to December 2014, sentinel hospital sites (12 in 2007, 10 in 2008, 15 in 2009, 14 in 2010, 15 in 2011, 12 in 2012, 15 in 2013, and 13 in 2014) in major population centres in 8 of the 10 provinces in Canada were recruited. These sites were geographically distributed in a population based fashion: (BC [1 site], Alberta [1 site], Saskatchewan [1 site], Manitoba [1 site], Ontario [3-5 sites], Quebec [2-4 sites], Maritimes [1-2 sites]).

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. The medical centres submitted "clinically significant" isolates from patients with a presumed infectious disease. Surveillance swabs, eye, ear, nose and throat swabs, as well as anaerobes, were excluded. 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. In 2007, 2008, 2009, 2010, 2011, 2012, 2013 and 2014; 7714, 5283, 5374, 4960, 3788, 2803, 3511, and 3174 isolates were collected, respectively (1,2).

Antimicrobial Susceptibilities: Following 2 subcultures from frozen stock, the in vitro activity of selected antimicrobials was determined by broth microdilution in accordance with the Clinical and Laboratory Standards Institute (CLSI) guidelines (CLSI, 2012 M7-A9). Antimicrobial MIC interpretive standards were defined according to CLSI breakpoints (M100-S24, 2014). Susceptibility testing could not be performed with all agents due to lack of space on the susceptibility panels. Antimicrobial agents were obtained as laboratory grade powders from their respective manufacturers. Stock solutions were prepared and dilutions made as described by CLSI (M7-A9, 2012). The MICs 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.

ACKNOWLEDGEMENTS

The authors would like to thank the investigators and laboratory site staff at each medical centre that participated in the CANWARD study.

The CANWARD study was supported in part by Abbott, Achaogen, Affinium, Astellas, Astra Zeneca, Bayer, Cerexa/Forest, Cubist, Galderma Laboratories, Merck, Paladin Labs, Pfizer/Wyeth, Sunovion, and The Medicines Company.

REFERENCES

- Zhanel GG, DeCorby M, Adam HJ, et al. 2010. Antimicrobial Agents and Chemotherapy; 54(11): 4684-4693.
- Zhanel GG, Adam HJ, Baxter M, et al. 2013. Journal of Antimicrobial Chemotherapy; 68 (Suppl 1): 7-22.

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

Organism (n) / Antimicrobial Agent	% S	% I	% R	MIC ₅₀	MIC (µg/mL)	Range
Staphylococcus aureus, MSSA (n=5990)						
Amikacin	99.2	0.4	0.3	4	≤ 2	> 64
Cefoxitin	99.5	0.5	0.4	4	0.12	> 32
Ciprofloxacin	86.2	3.0	10.8	0.5	4	0.06 - > 16
Clarithromycin	75.3	0.4	24.3	0.25	> 16	0.025 - > 16
Clindamycin	93.0	0.4	6.8	≤ 0.25	0.25	0.025 - 8
Daptomycin	100.0			0.25	0.25	< 0.06 - 1
Dapsone *				128	128	32 - 256
Doxycycline	99.0	0.7	0.3	≤ 0.25	0.25	> 16
Ertapenem	97.9	0.1	2.0	≤ 0.5	0.5	> 32
Levofloxacin	90.1	0.3	9.8	0.25	1	0.06 - > 32
Linezolid	99.98	0.02	2	2	0.12	> 8
Moxifloxacin	90.3	0.7	9.0	≤ 0.06	0.25	> 0.06 - > 16
Nitrofurantoin	100.0			16	16	0.5 - > 32
Tigecycline	99.9			0.12	0.25	0.03 - > 32
Tobramycin	97.2	0.2	2.6	≤ 0.5	0.5	0.5 - > 64
Trimethoprim Sulfam	99.4	0.6	0.8	≤ 0.12	0.12	> 8
Vancomycin	100.0			1	1	0.25 - > 2
Staphylococcus aureus, MRSA (n=1707)						
Amikacin	68.2	21.8	10.1	16	64	≤ 2 - > 64
Cefoxitin	0.1			99.9	> 32	> 32 - 1 - > 32
Ciprofloxacin	16.0	0.3	83.7	> 16	> 16	0.12 - > 16
Clarithromycin	14.4	0.4	85.2	> 16	> 16	0.025 - > 16
Clindamycin	52.8	0.1	47.2	≤ 0.25	> 8	0.025 - > 8
Daptomycin	99.9	0.1	0.1	0.25	0.5	> 16
Dapsone *				128	256	16 - 512
Doxycycline	97.6	0.8	1.5	≤ 0.12	1	0.12 - > 16
Gentamicin	92.2	0.3	7.5	≤ 0.5	1	0.5 - > 32
Levofloxacin	14.1		85.9	> 32	> 32	0.12 - > 32
Linezolid	100.0			2	2	0.12 - > 4
Moxifloxacin	16.7	3.2	80.2	8	> 16	0.06 - > 16
Nitrofurantoin	100.0			16	16	8 - > 32
Tigecycline	99.1			0.25	0.5	0.03 - > 32
Tobramycin	56.7	0.7	42.6	1	> 64	0.5 - > 64
Trimethoprim Sulfam	93.3	0.6	0.7	≤ 0.12	0.12	> 8
Vancomycin	99.9	0.1	0.1	1	1	0.25 - > 4
Staphylococcus epidermidis (n=775)						
Amikacin	95.2	2.9	2.0	≤ 2	16	≤ 2 - > 64
Amox-Clav				1	8	0.06 - > 32
Cefazolin				1	64	0.5 - > 128
Cefepime				4	> 32	> 1 - > 32
Cefotaxime				8	> 32	> 0.06 - > 32
Ceftriaxone				> 4	> 4	> 1 - > 4
Ciprofloxacin	44.9	1.6	53.6	4	> 16	0.06 - > 16
Clarithromycin	32.7	1.2	66.2	> 16	> 16	0.025 - > 16
Clindamycin	55.0	1.3	43.8	≤ 0.25	> 8	0.025 - > 8
Daptomycin	100.0			0.12	0.25	< 0.06 - 1
Dapsone *				128	512	32 - > 512
Doripenem				1	16	0.12 - > 32
Doxycycline	95.7	2.9	1.5	0.25	1	0.25 - > 32
Ertapenem				4	> 32	> 0.06 - > 32
Gentamicin				≤ 0.5	> 32	0.5 - > 32
Levofloxacin	44.2	1.6	54.2	4	> 32	0.12 - > 32
Linezolid	100.0			0.5	1	0.12 - > 4
Mercopenem				2	> 32	> 0.12 - > 32
Moxifloxacin	46.9	6.9	46.2	1	> 16	0.06 - > 16
Pip-Tazo				0.12	0.5	< 0.03 - 1
Tigecycline	99.3	12.8	27.8	2	64	0.5 - > 64
Tobramycin	59.4	0.4	40.6	1	8	0.12 - > 8
Trimethoprim Sulfam	100.0			1	2	0.25 - > 4
Vancomycin	100.0			1	1	0.25 - > 4
Streptococcus pneumoniae (n=2366)						
Amox-Clav	97.8	1.2	0.9	≤ 0.06	0.12	0.06 - > 16
Ceftriaxone *	99.3	0.5	0.2	≤ 0.12	0.12	> 16
Cefuroxime	93.6	1.8	4.6	≤ 0.25	0.5	0.25 - > 16
Chloramphenicol	98.5	4	2	2	2	0.12 - > 32
Ciprofloxacin	79.3	3.6	17.2	1	2	0.06 - > 16
Clarithromycin	92.9	0.6	6.5	≤ 0.12	0.12	> 16
Daptomycin				0.06	0.12	> 0.06 - > 32
Doripenem	99.9	0.1	0.1	0.06	0.06	< 0.06 - 2
Doxycycline	86.8	1.3	11.9	0.25	1	0.25 - > 16
Ertapenem	98.9	1.1	0.0	≤ 0.06	0.12	0.06 - 4
Imipenem	93.6	4.2	2.3	≤ 0.03	0.03	> 0.12 - 1
Levofloxacin	98.9	0.2	0.9	≤ 0.06	0.12	> 32
Linezolid	100.0			1	1	0.12 - > 2
Mercopenem	95.1	3.0	1.9	≤ 0.06	0.06	< 0.06 - 2
Moxifloxacin	99.0	0.5	0.5	0.12	0.25	0.06 - 8
Nitrofurantoin	82.6	12.9	4.5	≤ 0.03	0.25	0.03 - > 8
Pip-Tazo				≤ 1	≤ 1	> 8
Tigecycline	99.8			0.03	0.06	< 0.03 - 0.25
Trimethoprim Sulfam	100.0	6.3	8.9	≤ 0.12	2	> 16 - > 8
Vancomycin	84.9	0.8	0.8	≤ 0.25	0.25	> 0.12 - > 1
Streptococcus pyogenes (n=547)						
Amox-Clav				0.06	0.06	< 0.06 - 0.5
Ceftriaxone	99.8	0.2	0.2	≤ 0.12	0.12	> 16
Cefuroxime				0.25	0.25	0.25 - 0.5
Chloramphenicol	98.8	1.2		2	4	0.5 - 8
Ciprofloxacin	98.1	2.1	8.8	0.5	1	0.06 - 8
Ceftazidime				0.03	0.5	> 0.03 - > 32
Clindamycin	98.4			1.6	≤ 0.12	0.12 - > 8
Daptomycin	100.0			0.06	0.12	< 0.06 - 0.25
Dapsone *				32	512	4 - > 512
Doripenem	100.0			0.06	0.06	< 0.06 - 0.12
Ertapenem				0.25	0.5	> 0.06 - > 32
Gentamicin	97.1			0.3	0.12	0.12 - > 16
Levofloxacin	99.8	0.2	0.4	0.5	1	0.12 - > 4
Linezolid	99.6			≤ 0.06	0.06	< 0.06 - 0.12
Moxifloxacin	100.0			0.12	0.25	0.06 - 0.5
Nitrofurantoin	99.1			0.03	0.03	< 0.03 - 0.12
Pip-Tazo	100.0			≤ 1	≤ 1	> 16 - > 8
Tigecycline	100.0			0.03	0.06	< 0.03 - 0.25
Trimethoprim Sulfam	99.8			≤ 0.12	0.12	> 8
Vancomycin	100.0			0.5	0.5	0.25 - > 1
Enterococcus faecalis (n=1059)						
Amox-Clav	60.1	10.0	29.9	0.5	1	0.06 - > 32
Ciprofloxacin				1	> 16	0.25 - > 16
Clarithromycin				2	> 16	0.25 - > 16
Daptomycin	100.0			0.5	1	0.06 - 4
Dapsone *				256	512	8 - > 512
Doripenem	37.8	41.4	20.8	4	4	0.06 - > 32
Doxycycline				8	16	> 0.12 - > 32
Ertapenem				8	16	0.25 - > 32
Levofloxacin	65.6	1.1	33.3	2	> 32	0.25 - > 32
Linezolid	96.3	3.8	2	2	2	0.5 - > 1
Mercopenem				8	8	0.06 - > 32
Moxifloxacin				0.25	16	0.06 - > 16
Nitrofurantoin	99.6	0.4		8	8	2 - > 64
Pip-Tazo				4	8	> 1 - > 512
Tigecycline	98.0			0.12	0.25	< 0.03 - 1
Trimethoprim Sulfam	100.0			≤ 0.12	0.5	> 0.12 - > 8
Vancomycin	100.0			1	2	0.25 - > 4
Enterococcus faecium (n=400)						
Amox-Clav				> 32	> 32	0.06 - > 32
Ciprofloxacin	7.1	1.8	91.1	> 16	> 16	0.25 - > 16
Clarithromycin				> 16	> 16	0.03 - > 16
Daptomycin	100.0			1	2	≤ 0.03 - >