AMMI Canada – CACMID 2018

PF23

www.can-r.ca

Antimicrobial Resistance in Pathogens Isolated from Patients in Canadian Hospitals: CANWARD 2017

M. BAXTER[1], H.J. ADAM[1,2], M. McCRACKEN[3], A. DENISUIK[1], G. R. GOLDING[1,3], J.A. KARLOWSKY[1,2], D.J. HOBAN[1,2] and G.G. ZHANEL[1]

[1]University of Manitoba, [2]Shared Health, and [3]National Microbiology Laboratory, Winnipeg, Manitoba, Canada

Melanie Baxter
Microbiology, Health Sciences Centre
MS673-820 Sherbrook St.
Winnipeg, MB R3A 1R9
Email: meldecorby@yahoo.com

Introduction

Infections caused by antimicrobial resistant pathogens are a serious issue in Canada, and many parts of the world. Resistant pathogens include methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin resistant enterococci (VRE), *Escherichia coli* and *Klebsiella* species resistant to extended-spectrum β-lactams, penicillin-resistant *Streptococcus pneumoniae*, and carbapenem-resistant Enterobacteriaceae and *Pseudomonas aeruginosa*. Treatment options for these infections are often limited as these pathogens are frequently multidrug-resistant.

The ongoing goals of the CANWARD study are to assess pathogens associated with, and antimicrobial resistance patterns in respiratory, skin/skin structure, urinary and blood isolates in Canadian hospitalized patients on medical/surgical wards, emergency rooms (ER) and intensive care units.

Materials and Methods

Participating Sites: Fourteen hospital sites in major population centres in 8 of the 10 provinces in Canada were recruited. 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. From January through October 2017, each study site submitted clinical isolates (consecutive, one per patient) from inpatients/outpatients with respiratory (100), urine (25), wound (25), and bloodstream (10/month x 10 months) infections. Isolates were shipped on Amies semi-solid transport media to the coordinating laboratory, subcultured onto appropriate media, and stocked in skim milk at -80˚ C until minimum inhibitory concentration (MIC) testing was carried out. Characterization of MRSA isolates (*spa* typing) and putative VRE isolates (*van* PCR analysis) was performed at the National Microbiology Laboratory. In 2017, a total of 3,419 isolates were collected for the primary objectives of CANWARD.

Antimicrobial Susceptibility Testing: The *in vitro* activity of antimicrobials was determined by broth microdilution in accordance with the Clinical and Laboratory Standards Institute (CLSI) guidelines (M7-A10, 2015). Antimicrobial MIC interpretive standards were defined according to CLSI (M100, 28th Ed.). The MICs of the antimicrobial agents were determined using 96-well custom designed microtitre plates. These contained doubling antimicrobial dilutions in 100µl/well of cation adjusted Mueller-Hinton broth, inoculated to achieve a final concentration of ~5 x 10^5 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 recommended ATCC organisms.

Results

Table 1. Top Pathogens Isolated in Canadian Hospitals in 2017

Rank	Organism	n	% of Total
1	*Escherichia coli*	649	19.0
2	*Staphylococcus aureus, MSSA*	606	17.7
3	*Pseudomonas aeruginosa*	372	10.9
4	*Klebsiella pneumoniae*	244	7.1
5	*Haemophilus influenzae*	145	4.2
6	*Enterobacter cloacae complex*	119	3.5
7	*Streptococcus pneumoniae*	117	3.4
8	*Staphylococcus aureus, MRSA*	115	3.4
9	*Enterococcus faecalis*	99	2.9
10	*Stenotrophomonas maltophilia*	85	2.5
11	CNS / *Staphylococcus epidermidis*	82	2.4
12	*Klebsiella oxytoca/Raoultella spp.*	73	2.1
13	*Serratia marcescens*	62	1.8
14	*Streptococcus agalactiae*	54	1.6
15	*Streptococcus pyogenes*	48	1.4
16	*Enterococcus faecium*	46	1.3
17	*Proteus mirabilis*	43	1.3
18	*Haemophilus parainfluenzae*	31	0.9
19	*Enterobacter aerogenes*	27	0.8
20	*Candida albicans*	26	0.8
	Other	376	11.0
		3,419	

Figure 1. Patient Demographics by Hospital Location, Source, Gender, and Age Group (% of Total)

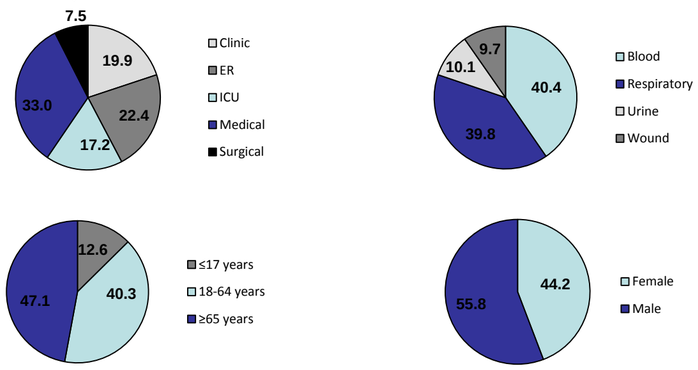

Table 3. Regional Prevalence (%) of MRSA, VRE and ESBL *E.coli*

Phenotype / Region	West	Ontario	Quebec	Maritimes	National
ESBL *E. coli* (n)	22	28	18	4	72
Total *E.coli* (n)	169	175	210	95	649
Prevalence ESBL *E. coli*	**13.0**	**16.0**	**8.6**	**4.2**	**11.1**
Total MRSA (n)	55	38	12	10	115
CA-MRSA (n)	32	22	3	5	62
HA-MRSA (n)	23	16	9	5	53
Prevalence MRSA	**20.8**	**18.9**	**7.7**	**9.9**	**16.0**
% CA-MRSA	58.2	57.9	25.0	50.0	53.9
% HA-MRSA	41.8	42.1	75.0	50.0	46.1
VRE (n)	3	5	0	0	8
Prevalence VRE (8 vanA *E. faecium*)	**6.5**	**14.3**	**0**	**0**	**5.5**

Table 2. Antimicrobial Activities Against Common Gram Negative and Gram Positive Pathogens Collected in 2017

Antimicrobial Agent	% S	% I	% R	MIC µg/mL MIC_{50}	MIC_{90}	Range Min	Range Max
***Escherichia coli* (n=649)**							
Amoxicillin Clavulanate	74.1	17.9	8.0	8	16	1	> 32
Cefepime	89.4	3.1	7.6	≤ 0.25	4	≤ 0.25	> 64
Ceftriaxone	86.9	0.6	12.5	≤ 0.25	> 64	≤ 0.25	> 64
Ciprofloxacin	74.1		25.9	≤ 0.06	> 16	≤ 0.06	> 16
Colistin[a]	99.4		0.6	0.25	0.5	0.12	4
Ertapenem	99.2	0.5	0.3	≤ 0.03	≤ 0.03	≤ 0.03	4
Gentamicin	92.1	0.2	7.7	≤ 0.5	2	≤ 0.5	> 32
Meropenem	99.8	0.2		≤ 0.03	≤ 0.03	≤ 0.03	2
Nitrofurantoin	98.0	1.4	0.6	16	32	1	> 512
Piperacillin-Tazobactam	95.5	2.5	2.0	2	8	≤ 1	> 512
Tigecycline*	100			0.25	0.5	≤ 0.03	2
Tobramycin	91.7	2.6	5.7	≤ 0.5	4	≤ 0.5	> 64
Trimethoprim Sulfa	73.5		26.5	≤ 0.12	> 8	≤ 0.12	> 8
***Pseudomonas aeruginosa* (n=372)**							
Amikacin	94.4	1.3	4.3	4	16	≤ 1	> 64
Cefepime	83.1	8.9	8.1	4	16	≤ 0.25	> 64
Ceftazidime	74.7	10.0	15.4	4	> 32	≤ 0.25	> 32
Ceftolozane-Tazobactam	96.2	2.7	1.1	1	2	≤ 0.12	> 64
Ciprofloxacin	83.6	5.4	11.0	0.25	4	≤ 0.06	> 16
Colistin	98.7		1.3	1	1	0.12	> 16
Gentamicin	89.8	4.8	5.4	2	8	≤ 0.5	> 32
Meropenem	82.0	4.3	13.7	1	8	≤ 0.03	> 32
Piperacillin-Tazobactam	79.6	9.4	11.0	8	128	≤ 1	> 512
***Staphylococcus aureus*, MRSA (n=115)**							
Ceftobiprole[a]	100			1	2	0.25	2
Ciprofloxacin	31.3		68.7	16	> 16	0.25	> 16
Clarithromycin	21.7		78.3	> 32	> 32	0.06	> 32
Clindamycin	75.7		24.3	≤ 0.12	> 8	≤ 0.12	> 8
Daptomycin	100			0.5	0.5	0.12	1
Gentamicin	97.4	0.9	1.7	≤ 0.5	≤ 0.5	≤ 0.5	> 32
Linezolid	100			2	4	0.5	4
Moxifloxacin	29.6	6.1	64.3	2	> 16	≤ 0.06	> 16
Tigecycline*	98.3			0.25	0.5	0.06	1
Trimethoprim Sulfa	98.3		1.7	≤ 0.12	≤ 0.12	≤ 0.12	> 8
Vancomycin	100			1	1	0.5	1
***Staphylococcus aureus*, MSSA (n=605)**							
Ceftobiprole[a]	100			0.5	0.5	≤ 0.06	1
Ciprofloxacin	86.3	4.5	9.3	0.5	2	0.12	> 16
Clarithromycin	72.4	1.5	26.1	0.25	> 32	0.06	> 32
Clindamycin	94.5	0.3	5.1	≤ 0.12	≤ 0.12	≤ 0.12	> 8
Daptomycin	99.8		0.2	0.5	0.5	0.12	2
Gentamicin	98.5		1.5	≤ 0.5	≤ 0.5	≤ 0.5	> 32
Linezolid	100			2	2	0.5	4
Moxifloxacin	91.9	0.7	7.4	≤ 0.06	0.25	≤ 0.06	> 16
Tigecycline*	99.0			0.25	0.25	0.06	1
Trimethoprim Sulfa	100			≤ 0.12	≤ 0.12	≤ 0.12	2
Vancomycin	100			1	1	0.25	2
***Streptococcus pneumoniae* (n=115)**							
Ceftriaxone	100			≤ 0.12	0.25	≤ 0.12	1
Cefuroxime[b]	90.1	1.8	8.1	≤ 0.25	0.5	≤ 0.25	8
Clarithromycin	80.0	2.6	17.4	≤ 0.03	2	≤ 0.03	32
Clindamycin	90.4	0.9	8.7	≤ 0.12	0.25	≤ 0.12	> 64
Doxycycline	88.7		11.3	≤ 0.25	4	≤ 0.25	16
Levofloxacin	100			1	1	0.5	2
Penicillin[b]	83.5	9.6	7.0	≤ 0.03	0.25	≤ 0.03	2
Trimethoprim Sulfa	85.2	4.3	10.4	0.25	4	≤ 0.12	> 8

* FDA breakpoints used for tigecycline; [a] Breakpoints defined by EUCAST ; [b] CLSI oral breakpoints.

Acknowledgements

The authors would like to thank the participating centres, investigators and laboratory site staff for their continued support:
Vancouver General Hospital; University of Alberta Hospital; Royal University Hospital; London Health Sciences Centre; University Health Network & Mount Sinai Hospital; Hamilton Health Sciences; Children's Hospital of Eastern Ontario; CHRTR Pavillon Ste. Marie; Jewish General Hospital; Hôpital de la Cité de la Santé; L'Hôtel-Dieu de Québec; The Moncton Hospital; Queen Elizabeth II Health Sciences Centre.

Conclusions

- Of the 3,419 pathogens obtained, the most common were: *E. coli* 19.0%, *S. aureus* (MSSA) 17.7%, *P. aeruginosa* 10.9%, *K. pneumoniae* 7.1%, and *S. pneumoniae* 3.4%.
- For *E. coli,* susceptibility was greatest to tigecycline 100%, meropenem 99.8%, ertapenem 99.2%, and piperacillin-tazobactam 95.5%.
- For *P. aeruginosa,* susceptibility was greatest to colistin 98.7%, ceftolozane-tazobactam 96.2%, amikacin 94.4%, gentamicin 89.8%, and cefepime 83.1%.
- All MRSA isolates remained 100% susceptible to vancomycin, ceftobiprole, linezolid and daptomycin.
- Rates of ESBL-producing *E. coli* have increased significantly from 3.4% in 2007 to 11.1% in 2017.