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Vancomycin-Resistant Enterococci (VRE) in Canadian Hospitals: CANWARD 2007-2013

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ABSTRACT

Background: The purpose of this study was to assess the prevalence and determine the genotypes of VRE isolated from clinical specimens in Canadian hospitals.
Methods: 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. A total of 1927 *Enterococcus* spp. isolates were collected. Susceptibility testing was performed using CLSI broth microdilution methods. PCR was used to identify vancomycin-resistant genes *vanA* and *vanB*, and to confirm species of VRE as *E. faecium* or *E. faecalis*.
Results: Of the 1927 *Enterococcus* spp. isolated from the CANWARD study, 4.2% (80/1927) were identified as VRE. All 80 VRE isolates were identified as *E. faecium.* Over the study period, the national prevalence of VRE tripled from 1.8% in 2007 to 6.0% in 2013 (p = 0.03) and peaked at 7.6% in 2011. Of the VRE, 90% (n=72) carried the *vanA* gene and 10% (n=8) carried the *vanB* gene. The proportion of VRE possessing the *vanB* determinant decreased over the study period from 37.5% in 2007 to 0% in 2013. All VRE were resistant to ciprofloxacin, levofloxacin, and vancomycin. 70.6%, 86.3% and 100% of VRE were susceptible to doxycycline, linezolid and daptomycin, respectively. In comparison, 44.7%, 51.6%, 51.6%, 95.5% and 100% of vancomycin susceptible enterococci were susceptible to ciprofloxacin, levofloxacin, doxycycline, linezolid and daptomycin, respectively. The majority of isolates originated from blood (68.8%) followed by wound (15.0%), urine (13.7%) and respiratory specimens (2.5%). Most VRE were identified from medical wards (45%) followed by ICUs (32.5%), surgery wards (12.5%), emergency rooms (6.3%) and hospital clinics (3.7%). Patient demographics were as follows: 50/50% male/female, 1.3% ≤ 17 years, 52.5% 18-64 years and 46.3% ≥ 65 years.
Conclusions: The prevalence of VRE infections has tripled from 2007 to 2013 in Canadian hospitals from 1.8% to 6.0%. The majority of VRE were *vanA* positive *E. faecium*. The proportion of VRE possessing *vanB* decreased over the study period. Although treatment options are limited for infections caused by VRE, most remain susceptible to linezolid and daptomycin.

BACKGROUND

Enterococcus is an important nosocomial pathogen. It can be a challenging organism to treat due to increasing antibiotic resistance, in particular the emergence of vancomycin resistant *Enterococcus* spp (VRE) (1). VRE is an important cause of infections in the ICU and is associated with high morbidity and mortality (2). The first isolate of VRE reported in Canada was in 1993 (3) and the first published outbreak in Canada was in 1995 (4). Since then, reports have indicated that rates of VRE can range from 1.8% to 28.5% (3,4). Rates in Canada have typically been low and range from 1.8% (3) to 6.7% (6). In Canada, *van*A has been previously reported to be the dominant gene responsible for vancomycin resistance (5,6).

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 Microbank vials (Pro-lab Diagnostics, Richmond Hill Ont, Canada).
Antimicrobial Susceptibility Testing: Antimicrobial susceptibilities were determined via broth microdilution (CLSI).
DNA Methodology: PCR was used to detect vancomycin-resistant genes *vanA* and *vanB* and to confirm species *E. faecium* and *E. faecalis*.

RESULTS

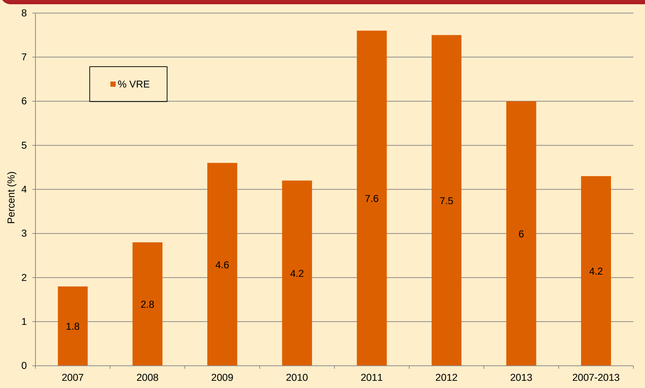

Figure 1. Proportion of *Enterococcus* spp (n=1927) with vancomycin resistance (n=80) observed in Canada from 2007-2013.

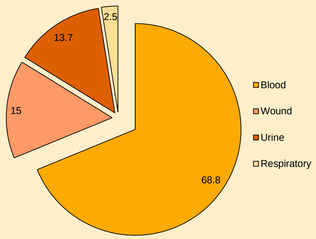

Figure 2: Distribution of specimens types where VRE was isolated

Table 1. Patient demographic information on clinical vancomycin resistant and vancomycin susceptible enterococci.

Demographics	VRE (N=80) N (%)	VSE (N=1847) N (%)
Gender		
Female	40 (50)	777 (42.1)
Male	40 (50)	1070 (57.9)
Age Group		
≤ 17 years	1 (1.3)	178 (9.6)
18-64 years	42 (52.5)	740 (40.1)
≥ 65 years	37 (46.3)	929 (50.3)
Location		
Hospital Clinic	3 (3.8)	237 (12.8)
Emergency Room	5 (6.3)	353 (19.1)
ICU	26 (32.5)	325 (17.6)
Medical	36 (45.0)	683 (37.0)
Surgical	10 (12.5)	249 (13.5)

Table 2. Antimicrobial susceptibility profiles (µg/mL) of vancomycin resistant *E. faecium*.

Antimicrobials	Breakpoint Interpretations (%)			Range of Values	MIC_{50}	MIC_{90}
	S	I	R			
Ciprofloxacin			100	>16	>16	>16
Levofloxacin			100	>32	>32	>32
Vancomycin			100	>32	>32	>32
Doxycycline	70.6	8.8	20.6	≤0.12-16	2	16
Linezolid	86.3	13.8		0.5-4	2	4
Daptomycin	100			≤0.06-2	1	2

[a]Note: %S – percent susceptible; %I – percent intermediate; %R – percent resistant.. Breakpoints (µg/mL): Ciprofloxacin Ss≤1, I-2, R≥4; Levofloxacin Ss≤2, I-4, R≥8; Vancomycin Ss≤4, I 8-16, R≥32; Linezolid Ss≤2, I-4, R≥8; Daptomycin Ss≤4.

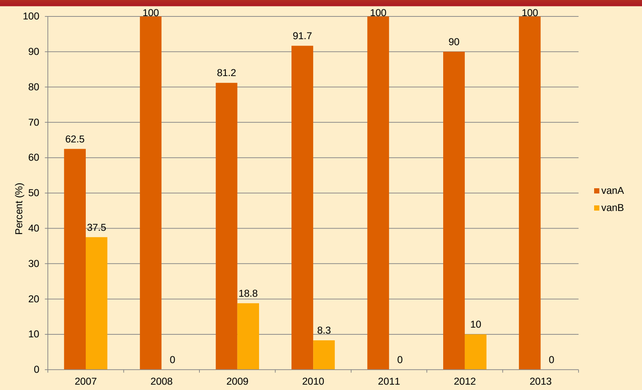

Figure 3. Distribution of VanA and VanB producing *E. faecium* from 2007-2013.

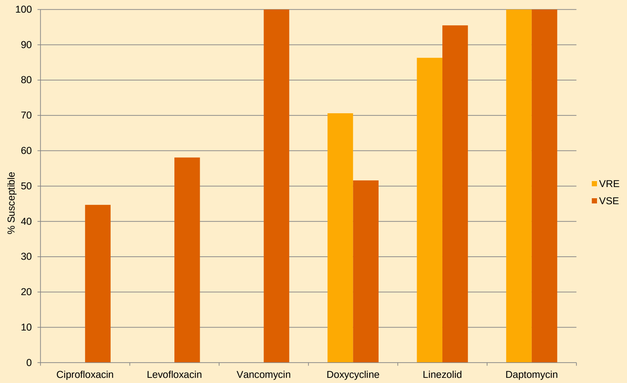

Figure 4: Antimicrobial susceptibility profiles of vancomycin resistant *E. faecium* (VRE) and vancomycin susceptible enterococci (VSE)

CONCLUSIONS

1. The prevalence of VRE infections has tripled from 2007 to 2013 in Canadian hospitals from 1.8% to 6.0%.
2. All VRE were *E. faecium* (100%).
3. *vanA* is the predominant genotype (90.0%) circulating in Canada.
4. The proportion of VRE possessing *vanB* decreased over the study period.
5. The majority from this study were blood culture isolates.
6. The most active agents against VRE were daptomycin and linezolid.

ACKNOWLEDGMENTS

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