Prevalence of Multi-Drug Resistant Organisms (MDROs) Using an Antibiotic Resistant Gene Assay at a Tertiary Care Center

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INTRODUCTION

Multi-drug resistant organisms (MDROs) continue to contribute to significant morbidity and mortality in hospitalized patients. In addition to MRSA and VRE, multi-drug resistant Enterobacteriaceae have become important causes of Hospital acquired infections. The prevalence of infections due to extended spectrum B-lactamases (ESBL) producing organisms and carbapenemase resistant Enterobacteriaceae (CRE) have increased dramatically. Efforts to reduce MDRO transmission in the healthcare setting warrants a combined approach that includes: hand hygiene, contact isolation and precautions, enhanced environmental cleaning, physician/patient education, as well as active surveillance cultures (ASC). ASC, as part of a combined infection prevention approach, has been successful with the reduction in transmission of MRSA, VRE, and with some MDR Gram negative rods. ASC has its disadvantages as there are delays in the reporting of culture results. Rapid diagnostic test that use molecular methodologies may be a reasonable approach in determining MDRO prevalence amongst hospitalized patients. The aim of this study was to perform active surveillance for MDROs at our metropolitan tertiary care center using the OpGen® Acuitas® MDRO Gene test. (http://opgen.com/mdro-services/acuitas-mdro-tests#Gene)

Materials and Methods

During a 3 consecutive day period in March 2016, we performed a cross sectional study to determine the prevalence of MDRO carriage amongst hospitalized patients at our tertiary care center in Washington, D.C. This study was performed in parallel with the Healthcare Antibiotic Resistance Prevalence in D.C.(HARP-DC) study. Eligible adult patients were enrolled after giving informed consent. Patients were excluded if they were unable to provide informed consent, unavailable due to procedural /diagnostic intervention, or located on a pediatrics, obstetrics/gynecology or psychiatric ward.

A peri-anal swab (BD Liquid Amies Elution Swab (ESwab) Collection and Transport System) was obtained on consenting adult patients, and the OpGen® Acuitas® MDRO Gene test (Gaithersburg, MD) was performed. This assay uses DNA sequence based technology and can detect seven antibiotic resistant gene families of ESBL producing organisms, CRE, carbapenemases and VRE. The resistance genes included: CTXM-1, CTXM-2, KPC, NDM-1, IMP-1, IMP-2, VIM-1, VIM-2, VIM-5, OXA-23, OXA-48, OXA-51, and VAN A (Table 2). Descriptive statistics were performed to determine the prevalence of the various MDRO genes in our hospitalized patient cohort. We also matched these patients with our Infection Prevention database to determine whether these patients had been on isolation at the time of the collection of the peri-anal specimens.

Table 1: Patient Demographics (n= 179)

Characteristic	Number	Percentage
Male	88	49.2%
Female	91	50.8%
Race (self-identified)		
Caucasian	67	37.4%
African American	86	48.0%
Other	26	14.5%
Transferred		
Outside Hospital	46	25.7 %
Nursing Home	4	2.2%
Transplant Recipient	21	11.7%
Days from Admission to Swab (Mean)	13.5	
ICU at time of swab	37	20.7%
ICU in past 6 months	67	37.4%
Antibiotic exposure in past 6 months	131	73.2%

Results

Table 2: MDRO genes

Gene	Comments
CTX-M- 1 , CTX-M- 2	ESBL; plasmid β-lactamase with increased activity against Cefotaxime as compared to other oxyimino-beta-lactam substrates
KPC	Klebsiella pneumonia carbapenemase; Ambler class A; plasmid mediated; confers resistant to all beta-lactams
NDM-1	New Delhi metallo-beta-lactamase; Ambler class B; mobile genetic element, plasmid mediated
IMP-1, IMP-2	Ambler class B; imipenemase; metallo- β-lactamase; chromosomal and plasmid acquired
VIM-1, VIM-2, VIM-5	Verona Integron-Mediated Metallo-β-lactamase; Ambler class B; seen in Pseudomonas
OXA-23, OXA-48	Oxacarbapenemase; Ambler class D; preferentially hydrolyzes oxacillin; plasmid mediated; responsible for carbapenem resistance in acinetobacter; OXA-48 associated with carbapenem resistance in Enterobacteriaceae
OXA-51*	Oxacarbapenemase; Ambler class D; preferentially hydrolyzes oxacillin; often chromosomally mediated; responsible for carbapenem resistance to acinetobacter
VanA	Vancomycin resistance; alteration in D-ala terminus to D-lactate; plasmid mediated; VRE

*The OXA-51 family represents beta lactamases very common to *A. baumannii* with little carbapenemase activity unless activated by an upstream transposon-encoded gene promoter

During the 3 day collection period, a total of 277 eligible hospitalized patients were identified; 43 patients declined; 31 were ineligible due to clinical, mental, emotional or language barriers; 22 unavailable due to diagnostic/therapeutic procedures; 2 specimens were not performed resulting in a total of 179 patients. Table 1 reveals the characteristics of the entire study population.

Of the 179 patients in the study, MDRO genes were isolated in 60 of them (33.5%). CRE genes were isolated in 8 patients (4.5%), non-CRE MDRO genes were isolated in 18 patients (10%), and the VanA gene was isolated in 45 patients (25.1%) (Figure1). The breakdown of specific MDRO genes identified in each of these patient groups is presented in Table 3.

Presence/carriage of the VanA genes was observed in a total of 11 patients who also had either CRE or non-CRE MDRO genes. This overlap is represented in Figure 2, which demonstrates that 7 of 8 samples with CRE genes also had the VanA gene (87.5%), while 4 of 18 samples with non-CRE MDRO genes also had the VanA gene (22.2%).

The percentage of patients that were on isolation at the time of the collection of the peri-anal specimens is shown in Figure 3. Only 28 of the 60 patients with positive MDRO genes (46.7%) were on isolation at the time of the peri-anal specimen collection. This figure also includes breakdown of isolation status based on MDRO gene isolation, which demonstrates that 8/8(100%) CRE gene positive patients, 2/18(11.1%) non-CRE MDRO gene positive patients, and 18/34 (52.9%) VanA positive patients were on isolation at the time of specimen collection.

All of the CRE gene positive patients were on isolation for another reason at the time of peri-anal specimen collection, which is represented in Table 4. This analysis shows that the CRE gene positive patients were on isolation for MRSA, VRE, or other MDR Gram negative rods.

Of the 60 patients with positive MDRO gene screening, 37 (61.7%) had prior hospitalizations, 30 (50%) had ICU stays in the previous 6 months, 52 (86.7%) were on antibiotics in the previous 6 months, and 13 (21.7%) were in the ICU at the time of sample collection. The average hospital length of stay before a positive MDRO gene screen specimen was obtained 22.8 days with a range of 1-195 days.

Figure 1: Presence of MDRO genes

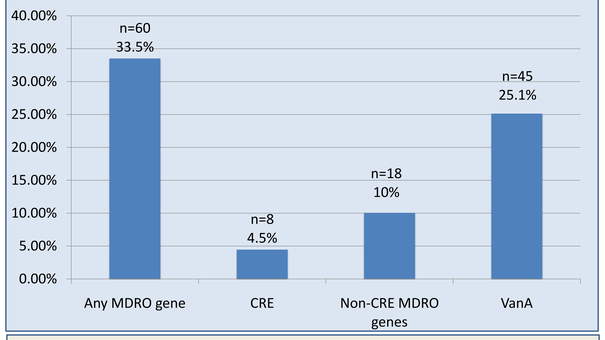

Table 3: Specific MDRO Genes Identified

Category	Genes
CRE n=8	6 KPC alone 1 KPC + OXA-23 1 KPC + OXA-48
Non-CRE MDRO genes n=18	6 CTX-M1 9 CTX-M2 2 OXA-51 1 OXA-23
VanA n=45	34 VanA alone 7 VanA + CRE genes 4 VanA + non-CRE MDRO genes

Figure 2: VanA Presence

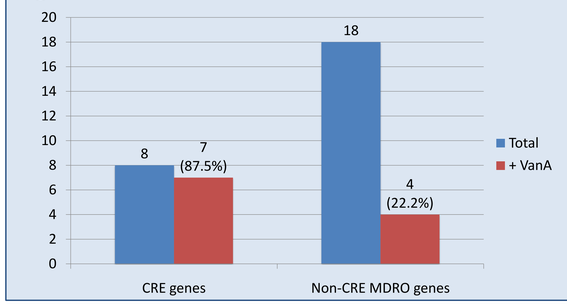

Figure 3: Percentage of Patients on Isolation

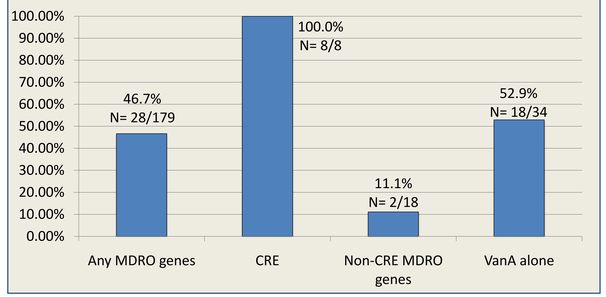

Table 4: Reason for Prior Isolation in CRE Gene Positive Patients

Number	MRSA	VRE	MDR Pseudomonas
1	X		
2	X	X	
3	X		
4			X
5		X	X
6	X		
7		X	
8		X	

Discussion

The current study was undertaken in order to determine the prevalence of MDROs amongst hospitalized patients at our tertiary care center. Based on our results over a 3-day collection period, 60 of 179 patients tested positive for MDRO by rapid gene testing, which represents a prevalence of 33.5%. Of these 60 patients, the highest proportion tested positive for the VanA gene (25.1% of the total population). CRE genes and non-CRE MDRO genes represented a significantly smaller proportion of the total MDRO gene prevalence (4.5% and 10%, respectively).

Using a rapid gene assay for MDRO surveillance, we indentified that 17.9% (32/179) of our hospitalized patients were not on contact isolation as they did not demonstrate clinical infection with an MDRO nor did they have a prior history of an MDRO. Our data also demonstrates that more than half of the patients (53.3%) who tested positive for MDRO genes were not on isolation at the time of specimen collection. Given the significant morbidity and mortality associated with infections due to MDROs in hospitalized patients, this is of great concern as these unidentified patients may serve as a reservoir for MDRO transmission within the hospital. Active surveillance by rapid MDRO gene testing may represent a potential screening method to decrease the rates of MDRO transmission amongst hospitalized patients.

Interestingly, all of the patients who tested positive for CRE genes were already on isolation for other reasons, including previous history of MRSA, VRE, or other MDR Gram negative rods. In our study, isolating patients with previous history of MDRO had the unforeseen benefit of also identifying all patients who tested positive for CRE genes. Therefore targeted surveillance using rapid gene testing in hospitalized patients with a prior history of MDROs may be a reasonable approach to identify potential unknown reservoirs of CRE and non-CRE MDR Gram negative rod infections.

Conclusions

- Using a rapid MDRO gene assay, we observed a 33.5% prevalence of MDRO carriage in our hospitalized patients
- 4.5% of hospitalized patients had occult CRE carriage using the rapid MDRO gene assay
- > 50% of patients with MDRO carriage were not on appropriate contact precautions at the time
- Rapid MDRO gene assay surveillance testing in hospitalized patients could potentially identify occult reservoirs of MDROs
- Use of this assay could potentially optimize infection prevention practices to decrease rates of transmission of MDROs in hospitalized patients