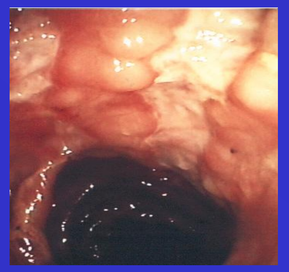

Hospitalized Patients with Ribotype 027 *Clostridium difficile* Infection and Stool Cytotoxicity Have More Severe Disease with an Increased Risk of Death

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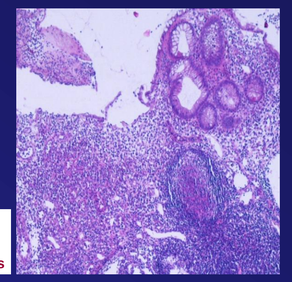


INTRODUCTION

Clostridium difficile **infection (CDI) accounts for 15 to 20% of antibiotic associated diarrhea and is the leading cause of hospital-acquired infectious diarrhea. In the United States, the mortality rate has increased from 5.7 deaths per million population in 1999 to 23.7 deaths per million population in 2004. The emergence of restriction endonuclease BI, North American pulse-field type 1 and PCR-ribotype R027 (BI/NAP1/027) strain in early 2000s led to outbreaks of CDI linked to more severe disease and an increased death rate in older sicker hospitalized patients. In addition, R027 infected patients suffer more frequent visits to the ICU and experience higher relapse rates. A combination of high toxin production, increased sporulation and resistance to fluorquinolones all support the increased virulence and spread of this strain. Cases of R027 CDI continue to increase with rates reaching over 40% for hospitals in the eastern U.S. However, some studies report a lack of association between R027 CDI and more severe disease raising questions on what cofactors contribute to poor outcomes. Further investigation is needed to identify the risk factors for severe disease to optimize treatment and improve patient outcome.**

AIM

In this study, we evaluated clinical and diagnostic indicators of severe CDI and their associations with poor outcomes including intensive care and mortality.

METHODS

- **211 patients suspected of CDI that were *tcdB* positive by real-time PCR were recruited under IRB approved protocol HSR-IRB# 13630 at the Medical Center of University of Virginia.**
- **Chart reviews: Co-morbidities, visits to ICU and mortality were collected as part of this study.**
- **Blood Analysis: White blood cell count (WBC), serum albumin and creatinine were analyzed at diagnosis by the clinical laboratory.**
- **Tissue culture: Human foreskin cell monolayers and toxin B neutralizing sera were used for specific neutralization with feces and toxigenic culture.**
- **Bacterial and toxigenic culture: Ethanol spore selection with CCFA was used to identify culture-positive specimens. Isolates were subcultured to BHI and grown for 72h then tested by tissue culture for the presence of toxin B.**
- **PCR ribotyping analysis: DNA was extracted from broth cultures using the QIAamp Mini Kit (Qiagen, Valencia, CA) and results were compared to a standard ribotype library.**
- ***IBD-SCAN®*: A quantitative ELISA for measuring stool lactoferrin concentration (µg/mL).**
- **Statistical analysis: Significance testing for percentage differences was based on Fisher's Exact Test. Significance tests for continuous variables was done using Wilcoxon rank sum test.**

RESULTS

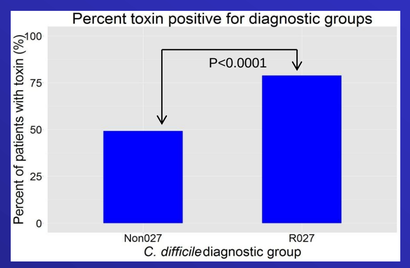
Table 1 Patient Characteristics	N	%	p-value*	total
Age in years, median (min,Q1,Q3,max)	62.0(18.0, 50.5, 72.0, 91.0)		<0.0001	211
<60	92	43.6		211
≥60	119	56.4		211
<65	118	55.9		211
≥65	93	44.1		211
Male gender	105	49.8	0.3350	211
Charlson index, median (min,Q1,Q3,max)	5.0(0.0, 3.0, 6.5, 14.0)		<0.0001	211
0	7	3.3		211
1-3	71	33.6		211
4-6	80	37.9		211
>7	53	25.1		211
Intensive care unit (ICU)	95	45	0.0032	211
100-day mortality (all cause)	50	23.7		211
Days until death, median (min,Q1,Q3,max)	47.5 (2.0 , 15.0, 114.8, 399.0)		<0.0001	67

*p-values for 100-day mortality (all cause)

Table 2 Diagnostic Variables	N	%	p-value*	total
PCR +	211	100		211
Tissue Culture +	129	61.1	0.1384	211
Toxigenic culture +	191	90.5	0.8048	211
Ribotype - 027	85	40.3	0.0315	211
White blood cell count, median(min,Q1,Q3,max)	11.5(0.2, 6.9, 16.6, 53.9)		0.0497	210
<10,000 10E3/mm3	89	42.4		210
10,000 - 15,000 10E3/mm3	52	24.8		210
>15,000 10E3/mm3	69	32.9		210
Lactoferrin, median (min,Q1,Q3,max)	49(0, 11, 234, 2823)		0.0438	211
<7.25, ug/g	49	23.2		211
7.25 - 100 ug/g	84	39.8		211
> 100 ug/g	78	37.0		211
Albumin level, median (min,Q1,Q3,max)	3.0(1.5, 2.5 ,3.4, 5.1)		0.0223	
<2.5 mg/dL	33	20.2		163
≥2.5 mg/dL	130	79.8		163
Creatinine, median (min,Q1,Q3,max)	1.0(0.4, 0.7, 1.6, 9.9)		0.0393	
<1.5 mg/dL	149	71.6		208
≥1.5 mg/dL	59	28.4		208

*p-values for 100-day mortality (all cause)

Figure 1.



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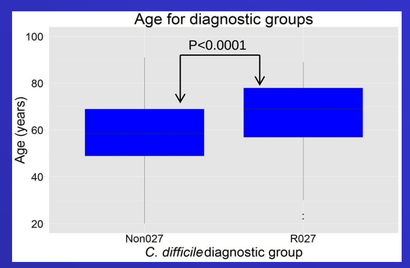

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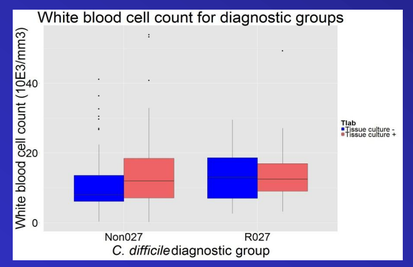

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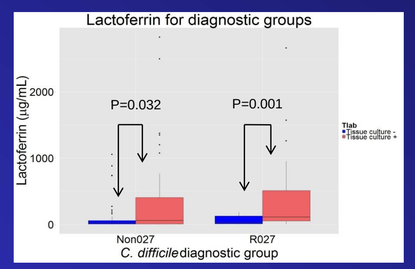

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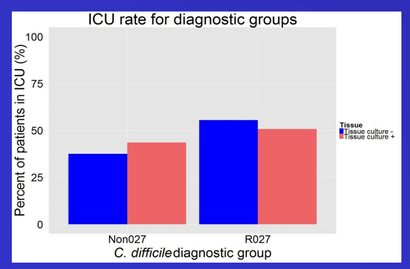

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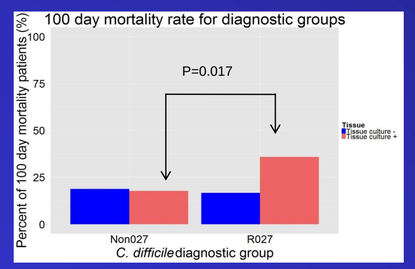

CONCLUSIONS

•Patients with R027 infection were older and had significantly more positive stool toxin.

•Lactoferrin was significantly higher in patients with positive stool toxin regardless of ribotype.

•Patients with R027 infection trended higher for ICU visits and those with positive stool toxin had a significantly higher mortality rate.

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