Severity and Clinical Outcomes of Clostridium difficile infection based on Toxin Assay Results

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Background

- Clostridium difficile infection (CDI) remains a major health problem in the US.
- The IDSA guidelines recommend using stool toxin assay as part of a multistep algorithm rather than nucleic acid amplification test (NAAT) alone. However, the clinical significance of toxin negative tests remains a subject of debate.
- We performed a prospective study in our institution to describe clinical outcomes of CDI based on the results of the stool toxin assay.

Methods

- Our lab utilizes a 2 step algorithm, using glutamate dehydrogenase plus detection of toxin A/B by enzyme immunoassay (EIA) arbitrated by NAAT for testing stool samples submitted for Clostridium difficile testing. The study was conducted between Jan-Dec 2017.
- Patients diagnosed with CDI based on lab results were divided into 2 groups based on toxin assay results.
- Shotgun metagenomics was performed directly on stool specimens using Illumina Next Seq in a subset of patients.
- Chart reviews were performed to assess clinical outcomes. Our primary outcome was incidence of severe CDI and 30-day mortality.

Results

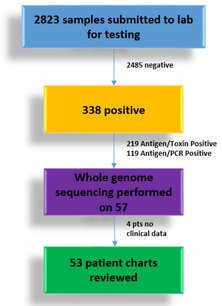


Figure 1: Flowchart of Patient Samples

Results

Table 1: Clinical Outcomes Based on Toxin Assay Results (53 pts)

	Toxin Positive	Toxin Negative/PCR Positive	p-value
No. of Patients	34	19	
Hospital Onset	10 (27%)	7 (37%)	0.57
Severe CDI	14 (41%)	8 (42%)	0.94
C diff Reads	0.17%	0.24%	0.70
30 day Mortality	1 (3%)	1 (5%)	0.67
NAP 1 Strains		2 (10.5%)	

Figure 2: Microbiome in Patients with Active CDI, Reads >50,000 (n=57)

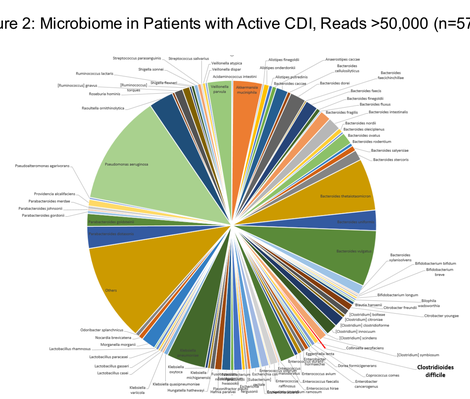
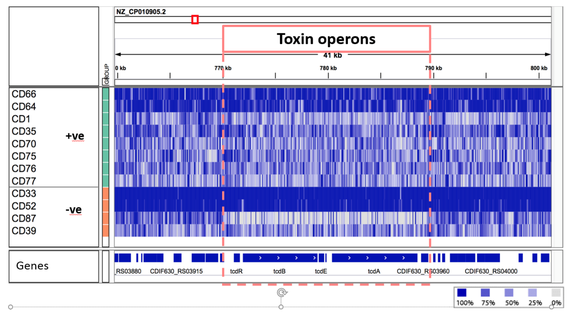
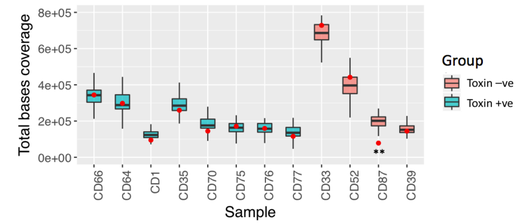


Figure 3: Genome coverage for the toxin operon within *C. difficile* genome (>80% coverage, n=12)



Results

Figure 4: Boxplot represents the distribution of total bases coverage of 100 random regions in the *C. difficile* genome.



- 21 samples had a high percentage of pathogenic gram negatives (9.8%-76.4% of total reads)
- CD87 show significantly loss of toxin operons in the *C. difficile* genome (with Student's T-test p-value < 3.0e-10 in random permutation tests with 100 iterations).

Conclusions

- In our cohort, detection of Clostridium difficile toxin in stool samples was not associated with increased severity of disease. Our cohort has a higher prevalence of patients on active chemotherapy than previously studied cohorts.
- Bioburden of Clostridium difficile was not significantly different in toxin positive and negative disease.
- High percentage of gram negatives were seen in 36% of CDI cases on sequencing

Acknowledgements

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