

Hospitalwide Asymptomatic and Symptomatic *Clostridium difficile* - Associated Disease (CDAD) Surveillance by Real-time PCR

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INTRODUCTION

- Nucleic acid amplification tests (NAATs) for *C. difficile* (CD) toxin genes are increasingly being used for CDAD diagnosis.
- 35% of hospitals in the CDC National Healthcare Safety Network employ a NAAT for CDAD diagnosis.

OBJECTIVE

To assess the accuracy of real-time PCR for CDAD diagnosis with a hospitalwide real-time PCR surveillance for asymptomatic CD colonization and CDAD at a university hospital following a rise in CDAD incidence rates with NAAT initiation.

METHODS

Surveillance Study population: All adult patients in a large, university hospital in Houston, Texas were screened for enrollment from January 8 - 11, 2013. A stool sample or rectal swab was collected from each consenting subject.

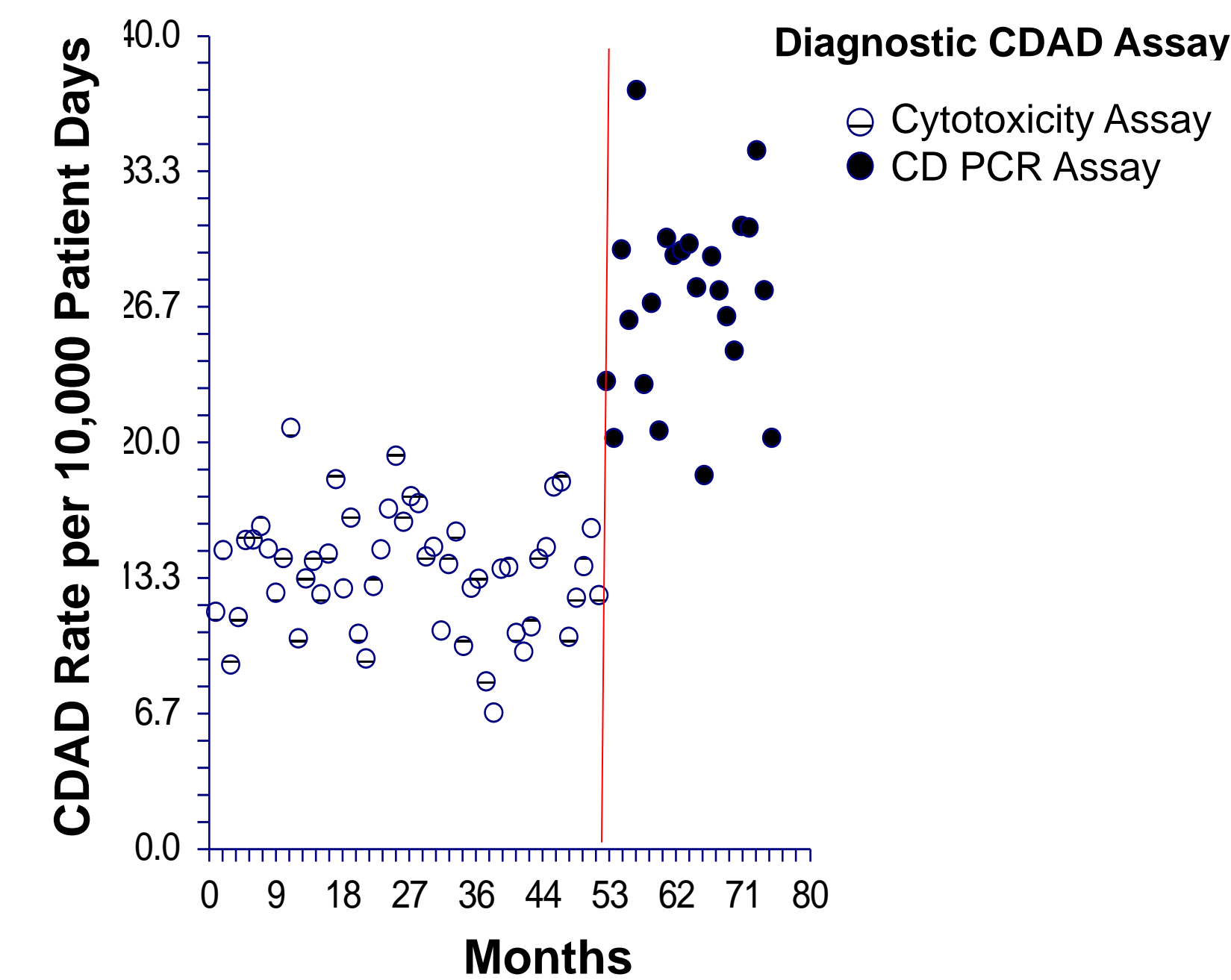
Definitions:

- 1) Diarrhea: ≥ 3 unformed stools within 24 hours.
- 2) CDAD: positive PCR, ELISA, or toxigenic culture with diarrhea.
- 3) Asymptomatic CD colonization: CD detection by PCR, ELISA, or toxigenic culture in the absence of diarrhea.

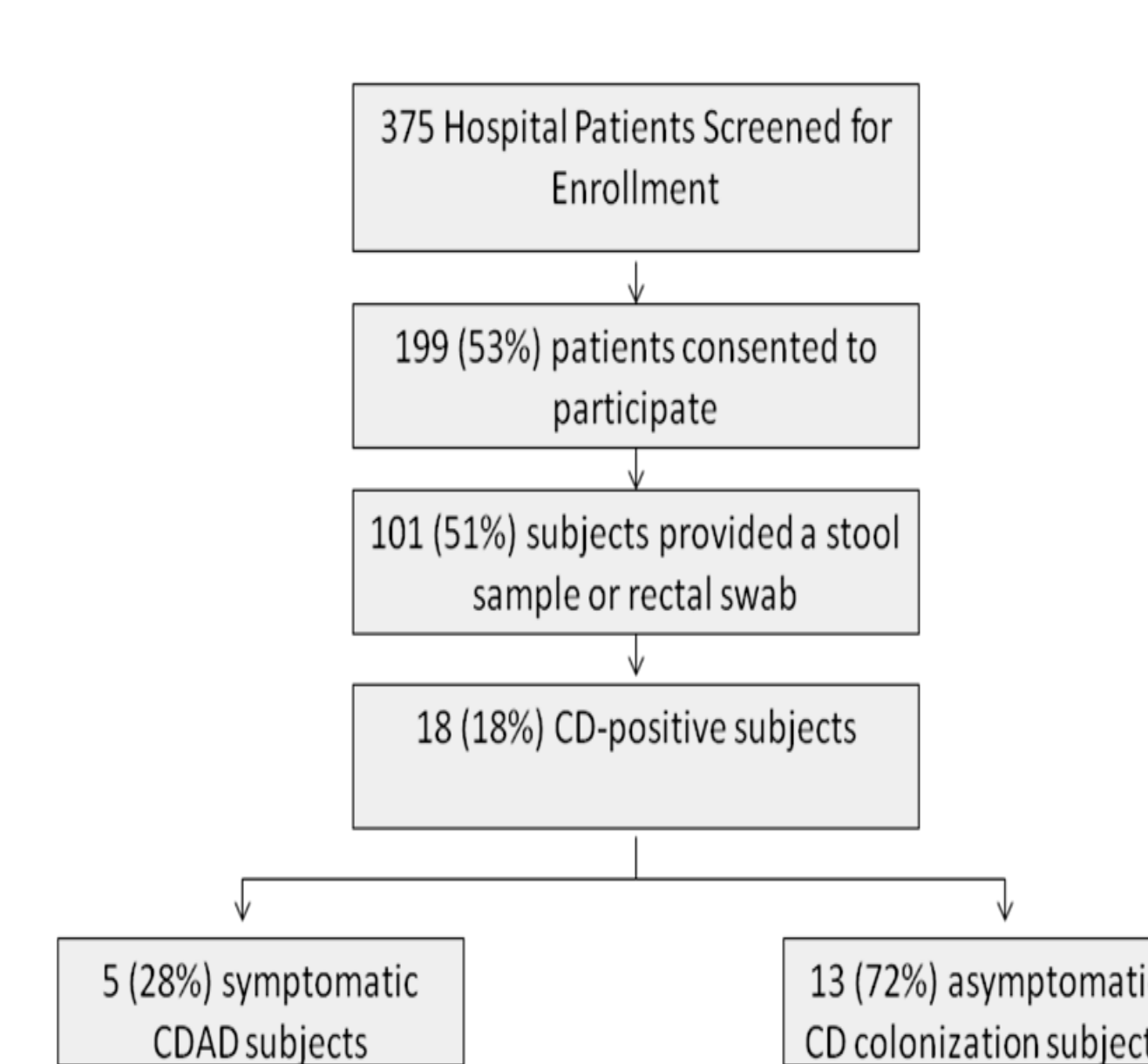
C. difficile Evaluation:

- 1) Real-time PCR for *tcdA* and *tcdB* genes
- 2) BD GeneOhm Cdiff PCR assay for *tcdB* gene
- 3) ELISA for toxins A and B (TECHLAB)
- 4) Anaerobic culture on CCFA plate with alcohol shock and conventional PCR for *tcdA* and *tcdB* genes

Figure 1. CDAD Incidence Density Rates Figure 2. Study Enrollment and Results



Note. January 2007 to March 2013 CDAD incidence density rates. PCR initiation was associated with increased CDAD rates ($p < 0.001$).



RESULTS

- Mean monthly hospital CD detection rate doubled from 13.4 per 10,000 patient days (May 2010-April 2011) to 27.0 per 10,000 patient days (May 2011-April 2012; $p < 0.001$) after PCR initiation.
- 199 hospitalized subjects were enrolled, from whom 101 fecal specimens were collected.
- *C. difficile* was detected in 18 (18%) subjects who provided a fecal sample.
- 5 CDAD subjects (5%) and 13 asymptomatic CD colonization subjects (13%) were identified ($p < 0.05$).
- No significant difference in host risk factors between CDAD subjects and CD colonized subjects except the mean number of stools passed in the previous 24 hours (5.6 ± 3.8 vs. 0.9 ± 0.8 stools, respectively, $p < 0.01$).

Table. Study Population Host Factors by *C. difficile* Status

	CD-Positive Subjects (n=18)	CD-Negative Subjects (n=83)	P Value	CDAD Subjects (n=5)	CD Colonized Subjects (n=13)	P Value
Mean Age \pm SD (yrs)	57.0 \pm 16.2	60.2 \pm 15.8	0.47	53.0 \pm 16.8	58.5 \pm 16.4	0.59
Male Gender – no. (%)	8 (44.4)	44 (54.3)	0.45	2 (40.0)	6 (46.2)	1.00
Residence in a healthcare facility within past 6 mo. – no. (%)	2 (11.1)	9 (11.4)	1.00	0	2 (15.4)	1.00
Hospitalized within past 3 mo. – no. (%)	7 (38.9)	35 (43.8)	0.71	2 (40.0)	5 (38.5)	1.00
Antibiotic use – no. (%)	11 (61.1)	56 (68.3)	0.56	2 (40.0)	9 (69.2)	0.33
Antacid use – no. (%)	7 (38.9)	37 (45.1)	0.63	2 (40.0)	5 (38.5)	1.00
History of previous CDAD – no. (%)	1 (5.6)	11 (13.6)	0.69	0	1 (7.7)	1.00
Mean no. stools in past 24 hours \pm SD	2.2 \pm 2.9	1.8 \pm 2.5	0.51	5.6 \pm 3.8	0.9 \pm 0.8	<0.01
Diarrhea within past 24 hours – no. (%)	5 (27.8)	10 (12.2)	0.09	---	---	---

CONCLUSIONS

- Majority of healthcare-associated diarrhea is not attributable to CDAD.
- The prevalence of asymptomatic *C. difficile* colonization exceeds CDAD rates in healthcare facilities.
- PCR detection of asymptomatic CD colonization among patients with non-CDAD diarrhea may be contributing to rising CDAD rates and a significant number of CDAD false-positives.
- Inappropriately diagnosed CDAD patients may be receiving unnecessary anti-CDAD therapy.
- PCR is inadequate as the sole diagnostic procedure for CDAD.
- Better methods are needed for CDAD diagnosis.