

Influence of *Chlamydia trachomatis* Organism Load on Reinfection Risk

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Introduction

- Genital *Chlamydia trachomatis* (CT) infection remains highly prevalent worldwide
 - CT infection rates are higher in women
 - Women have greater morbidity due to CT infection
- Detection of CT infection within months of initial diagnosis and treatment is a common occurrence (up to 20% in some studies).
 - Most repeat CT detection is due to CT reinfection
- CT reinfection likely contributes to sustaining the high CT infection prevalence
- Most studies evaluating predictors of CT reinfection have focused on epidemiological and behavioral factors

Objective

- Evaluate the influence of CT organism load on CT reinfection risk in women

Methods

- Clinical data and cervical swab specimens are being prospectively collected from CT-infected women ≥ 16 years of age at the Jefferson County Department of Health STD Clinic in Birmingham, AL, USA, as part of a CT natural history study
 - Women with gonorrhea, HIV infection, or prior hysterectomy are excluded
- Women are recruited at the time they return to the clinic for treatment of a positive CT screening test and are enrolled after providing written informed consent
- At enrollment, participants undergo a pelvic exam in which two cervical swabs are collected: one swab is for repeat CT testing by NAAT (Aptima Combo 2®, Hologic, Bedford, MA, USA) to confirm they are CT infected and the other swab is stored in M4® media (Remel, Lenexa, KS, USA) at -80°C
- Participants are treated with azithromycin 1g and scheduled for 3- and 6-month follow-up visits for repeat cervical NAAT and collection of an extra cervical swab
- CT organism load quantification from the stored cervical swab specimen is performed using real-time PCR (Cobas® 4800, Roche, Indianapolis, IN, USA)
 - To estimate organism load, a CT calibrator is run using stock CT samples with known organism counts to create cycle threshold standard curves for comparison with clinical samples, providing reliable and reproducible results that allow for relative quantification on a log scale
- Analyses are done with Stata (Stata Corp. Release 8.0, College Station, TX)
 - The relationship of participant characteristics and median \log_{10} CT load with CT reinfection (positive CT NAAT at the 3- or 6-month follow-up) is evaluated by Fisher's exact, Chi-squared, or Wilcoxon Rank Sum tests as appropriate

Results

- To date, 146 subjects had CT infection at enrollment, completed follow-up, and had CT load measured from the stored enrollment cervical swab sample

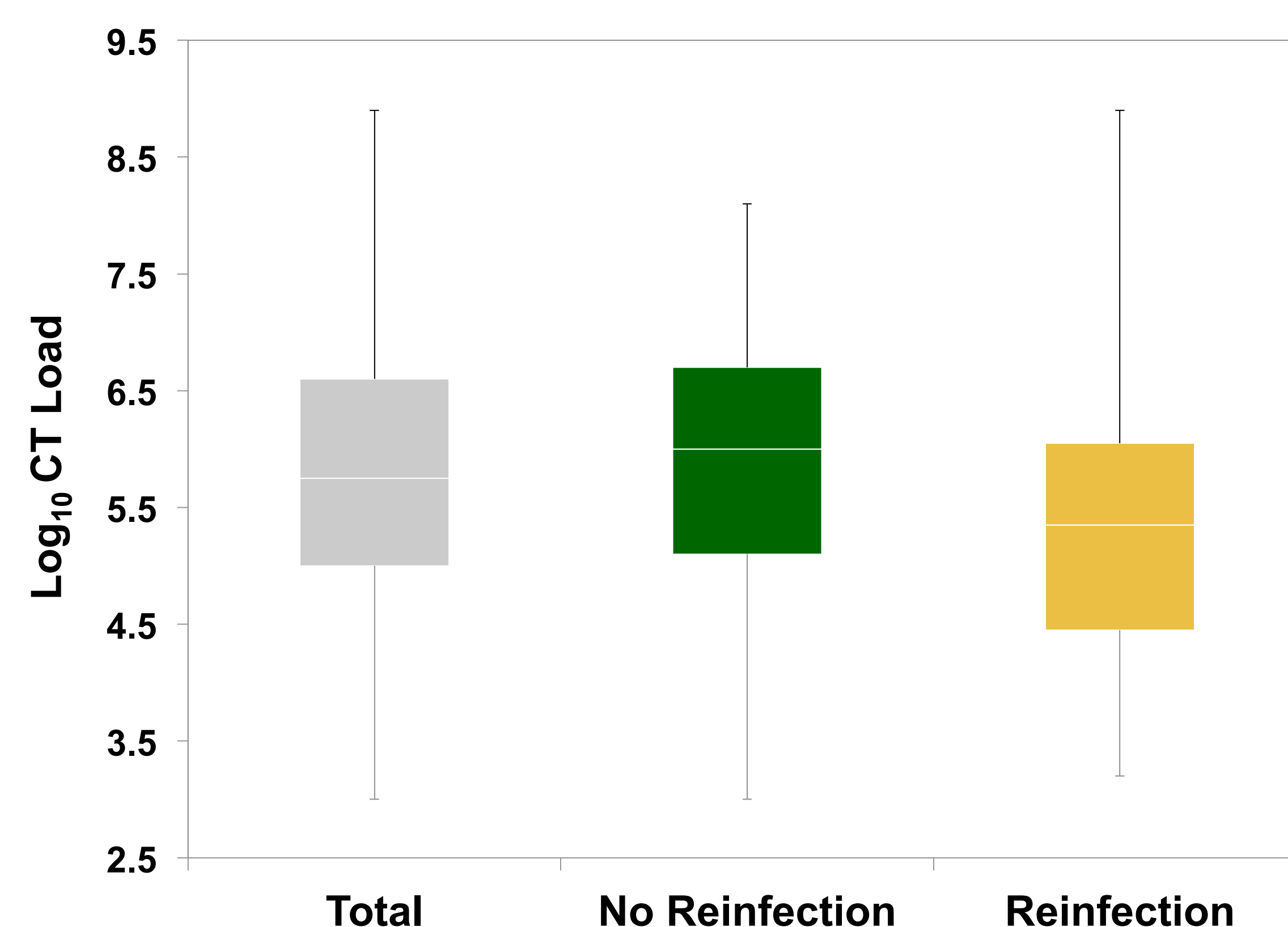
Table 1. Subject Characteristics at Enrollment (n=146)

Characteristic	n (%)
Median age	22 (range 16-50)
Race	
-African American	138 (95)
-Caucasian	6 (4)
-Other	2 (1)
Hispanic	2 (1)
Median sex partner # prior 3mo	1 (range 1-9)
No genital symptoms	68 (47)
Prior chlamydia - reported or documented*	77 (53)
Bacterial vaginosis	36 (25)
Vaginal candidiasis	21 (14)
Trichomoniasis	4 (3)
Cervicitis	36 (25)

*Missing data in 1 subject

- The median (range) \log_{10} CT load at enrollment was 5.75/mL (3 - 8.9/mL)
 - Median (range) \log_{10} CT load was higher in women with vs. without cervicitis (6.4 vs. 5.6, $P = 0.02$)
 - Median (range) \log_{10} CT load was higher in women with vs. without abdominal pain symptom (6.5 vs. 5.7, $P = 0.07$)
 - CT load did not differ by other enrollment subject characteristics
- CT reinfection at follow-up occurred in 28 (19%)
 - Reinfection was somewhat associated with younger median age (20.5 years in reinfection vs. 22 years in no reinfection; $P = 0.07$)
 - Reinfection occurred significantly less often in women with vs. without candidiasis (0% vs. 22%, $P = 0.01$)
 - Reinfection frequency did not differ by other enrollment subject characteristics

Enrollment Cervical \log_{10} CT Load, Stratified by CT Reinfection Status at Follow-Up



- **Findings:** Data shown as box-and-whiskers graph. The box extends from 25th to 75th percentile, with the median response indicated by the white line in the box. Whiskers represent the range. Women with reinfection at follow-up had a lower median cervical \log_{10} CT load at the time of treatment than women without reinfection (5.35 vs. 6, $P = 0.09$).

Conclusions

- CT organism load was higher in women with cervicitis
 - The higher CT load may elicit stronger inflammatory mucosal immune responses that contribute to cervical discharge and/or friability
- A lower cervical CT organism load at the time of treatment was associated with a greater CT reinfection risk
 - It is possible lower CT loads could elicit weaker protective cellular immune responses, predisposing to greater reinfection risk
 - The lower CT loads could reflect early CT infection, whereby treatment early in infection could impair immunity
- CT reinfection did not occur in women with candidiasis
 - This preliminary finding likely reflects the notion that an acidic pH genital mucosa is prohibitive to CT infection acquisition or persistence
- Our future studies will evaluate differences in CT load at the time of treatment vs. reinfection and influence of immune responses on CT load

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