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Chlamydia trachomatis infection and seropositivity in women reporting sexual contact to a chlamydia-infected partner

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Abstract

Among 73 women presenting to a STI clinic in Birmingham, Alabama for reported sexual contact to a chlamydia-infected partner, *Chlamydia trachomatis* was detected in genital specimens in 24 (32.8%), less often in women reporting prior chlamydial infection ($P = 0.001$). Most women (93.2%) were *C. trachomatis* seropositive.

Short Summary

Among 73 women presenting to an STI clinic for reported sexual contact to a chlamydia-infected partner, 32.8% had *Chlamydia trachomatis* detected in genital specimens and 93.1% were seropositive.

Keywords

chlamydia; contact; serology; partner; prevalence

INTRODUCTION

Chlamydia trachomatis (CT) infection remains the most prevalent bacterial sexually transmitted infection (STI).[1,2] CT detection and treatment in women is important to decrease CT-associated reproductive sequelae and to limit further CT transmission.[3,4] The Centers for Disease Control and Prevention (CDC) recommends annual CT screening with nucleic acid amplification tests (NAATs) for asymptomatic sexually active women aged <25 years and older women with risk factors as well as CT diagnostic testing with NAATs for symptomatic women.[4] CDC also recommends CT testing with NAAT and presumptive treatment (i.e., before test results become available) for women with recent sexual contact with a CT-infected partner;[4] however, some CT-exposed women test CT NAAT negative,[5–8] suggesting they were never infected or cleared their infection through natural immunity or incidental treatment.

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The extent that natural immunity develops in women following CT infection remains to be fully elucidated. Among treated CT-infected women, reinfection occurs in about 10%−20% within one year,[9] suggesting some do not develop protective immunity after infection. However, it has been reported that CT infections spontaneously resolve in about 50% of women within a year of detection,[10,11] and women with spontaneous CT resolution before treatment have lower reinfection rates,[12] suggesting some develop natural immunity to CT. Research studies on CT infection concordance within sexual partnerships have reported 43% −77% concordance for female partners of CT-infected males,[5–8] which also supports that some females may have protective immunity to CT.

Women reporting sexual contact to a CT-infected partner often present without their partner and receive presumptive treatment as part of sexual health management. A recent retrospective study of Seattle STI clinic longitudinal data on presumptive treatment for contacts to CT infection and/or gonorrhea reported that up to 43%−61% of women reporting contact to either STI were overtreated (i.e., tested negative).[13] Our prospective study sought to better understand the frequency of genital CT detection and CT seropositivity in women reporting sexual contact to a CT-infected partner.

MATERIALS AND METHODS

We prospectively enrolled a convenience sample of women ≥16 years of age who sought care at the Jefferson County Department of Health (JCDH) STI Clinic in Birmingham, Alabama, for a reported sexual contact to a CT-infected partner. Women who were pregnant, had a prior hysterectomy, were co-infected with HIV or had received antibiotics with anti-CT activity in the prior 30 days were excluded as these factors could affect CT detection and/or antibody responses. At enrollment, participants were interviewed and data were collected on demographics, sexual history, hormonal contraceptive use, antibiotic use, symptoms, and clinical findings. A pelvic examination was performed and a vaginal swab was collected for wet mount and endocervical swab for CT and *Neisseria gonorrhoeae* NAAT (Aptima Combo 2® Assay; Hologic, Inc., Marlborough, MA). Blood was collected from which serum was separated for antibody testing. Participants were treated with azithromycin 1g single dose. Participants returned for a 3-month follow-up visit in which blood was collected and sera separated and stored for future studies. The current study focuses on enrollment visit data and antibody testing from enrollment and 3-month visits. The study was approved by the University of Alabama at Birmingham (UAB) Institutional Review Board and JCDH and all women provided written informed consent before enrollment.

CT antibody testing was performed using a CT elementary body (EB) ELISA by reported methods.[14,15] Briefly, the ELISA used inactivated CT EBs pooled from serovars D, F, and J. CT-specific IgG1 and IgG3 responses were detected using alkaline phosphatase–labeled mouse antihuman IgG1 (SouthernBiotech, Birmingham, AL, and Cal Biochem, San Diego, CA) and mouse antihuman IgG3 (SouthernBiotech) at an optical density of 405 nm (OD_{405}). Cutoff OD_{405} values for positive IgG1 and IgG3 anti-CT responses were >0.35 and >0.1, respectively. Sera were run in triplicate at a 1:32 dilution. Seropositivity was defined as a

positive IgG1 or IgG3 response. The EB ELISA has a high sensitivity (≥90%), and antibody cross-reactivity with *C. pneumoniae* is not a concern.[15,16]

Differences in demographic, clinical, and behavioral characteristics as well as seropositivity and magnitude of antibody responses between women with versus without a positive CT NAAT were analyzed with Stata (version 14.0, StataCorp, College Station, TX) using Fisher's exact test and Wilcoxon rank sum tests as appropriate; $P < 0.05$ was used as the cutoff for statistical significance. For significant associations, prevalence ratios with 95% confidence intervals were determined using SAS (version 9.4, SAS Institute Inc., Cary, NC).

RESULTS

From March 2015 to March 2018, 73 women were enrolled. Their median age was 22 years (interquartile range [IQR], 20–26), 83.6% were African American, and 1.4% were Hispanic (Table 1). The median sexual partner number reported in the prior 3 months was 1 (IQR, 1–2) and number of days since last sexual activity was 7 (IQR, 3–14). Prior CT infection was self-reported by 57.5%. About half of women were asymptomatic, and cervicitis was diagnosed in 6.8%. Other urogenital infections were highly prevalent: 43.8% had bacterial vaginosis, 10.9% trichomoniasis, 10.9% vulvovaginal candidiasis, and 8.2% gonorrhea.

CT NAAT was positive in 24 (32.8%) women. CT NAAT positive women reported prior CT infection less often (29.2% vs. 71.4%; prevalence ratio [PR], 0.40; 95% confidence interval [CI], 0.24–0.67) and more often had cervicitis (20.8% vs. 0%; PR, 1.26; 95% CI, 1.03–1.55) (Table 1). CT NAAT positivity was not significantly associated with other participant characteristics, including number of days since last sexual activity.

Most women (68 [93.2%]) were CT seropositive at enrollment. The 5 women who were seronegative at enrollment (also CT NAAT negative) were also seronegative at their 3-month visit (confirming they were never CT infected). There was no significant difference in CT NAAT positivity based on CT serostatus ($P = 0.16$). Among those who were CT seropositive, there was no significant difference in the magnitude of the antibody response at the enrollment visit in those who were CT NAAT positive vs. negative: Median IgG1 OD_{405} 3.275 vs. 3.237 ($P = 0.92$) and median IgG3 OD_{405} 1.302 vs. 1.181 ($P = 0.22$).

DISCUSSION

Women presenting as a sexual contact to a CT-infected partner are routinely provided empiric CT treatment, but there are limited data on how often such women have active CT infection. We investigated how often such women seen in an STI clinic had CT detected and found that only about one-third tested CT NAAT positive, which is lower than the CT NAAT positivity frequency in CT-exposed women reported in previous CT concordance studies that tested both sexual partners (ranged 43%−77%).[5–8] These partner studies found lower concordance rates when the index CT-infected patient was only positive by CT NAAT and not by lower sensitivity culture, which suggests CT load may impact transmission risk. Our study did not have access to partners to test CT load, which could have provided some insight into the lower CT NAAT positivity in our study. It is possible that our cohort may have had a higher frequency of prior CT infections than cohorts from earlier studies and

this could impact CT NAAT positivity, but this could not be determined from earlier studies because they did not evaluate seropositivity. It is also possible our small sample size, the convenience sampling enrollment approach, and condom use in these women (data which we did not collect) could also have impacted the precision of our CT NAAT positivity rate.

One possible explanation for women reporting sexual contact to a CT-infected partner being CT NAAT negative is that they had protective immunity develop following previous CT infection and were either not infected or were infected but cleared infection quickly.[17] This is supported by our finding that women testing CT NAAT negative more often reported prior CT infection, although it was self-reported and not confirmed. However, while only 57.5% reported prior CT infection, 93% were seropositive, indicating many were unaware of having previous CT infection, which is not uncommon based on a recent CT seroprevalence study we published.[18] Among women in our current study who denied prior CT infection, 87% were seropositive, which reflects the high CT risk of our study population. One possible reason that CT NAAT negativity was associated with reported prior CT infection is that women reporting prior CT infection may have had more prior CT infections, which could strenghten their protective immunity. We previously found in this population that repeated CT infection was associated with lower CT loads.[19] There also could be recall bias in that they may be more likely to recall a prior CT infection if it was recent and a more recent infection could provide stronger protective immunity. While we did not find differences in magnitude of antibody responses by CT NAAT status, we did not measure functional antibody responses (e.g., neutralizing antibodies). Understanding functional humoral and cellular immune responses in women reporting sexual contact to a CT-infected partner that are CT NAAT negative could provide insight into protective immunity to CT that would be valuable for vaccine development efforts. It is also worth noting that another possible reason that CT NAAT negativity was associated with reported prior CT infection is that women reporting prior CT infection may have safer sexual behaviors, including being more inclined to use condoms.

Another possible explanation for women reporting sexual contact to a CT-infected partner being CT NAAT negative is that they were never exposed to CT. Our finding that 5 (7%) women were CT seronegative and remained so 3 months later supports the possibility they might not have been exposed, but it’s still possible that they were exposed and just not infected because the CT load they were exposed to was too low and/or because they were using condoms. We did not have their sexual partners’ sexual history or test results to further address the CT exposure.

A clinical implication of findings from our studies and others[5–8,13] is that many women reporting sexual contact to a CT-infected partner did not have evidence supporting active CT infection and were overtreated, which exposed them to potential adverse effects of treatment and could contribute to antimicrobial resistance development. Availability of rapid, accurate point of care tests will reduce overtreatment of contacts to CT and such tests are expected to become available in the next few years.

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Potential conflicts of interest:.

BVDP reports receiving honorarium, consulting fees, or research support paid to her institution from Abbott Molecular, binx health, BD Diagnostics, BioFire, Cepheid, Hologic, Rheonix, Roche Molecular Systems, Inc and SpeeDx. WMG reports receiving honoraria from Hologic, Inc. and Sanofi, and research support paid to his institution by Hologic, Inc.

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Table 1.

Characteristics of Women Reporting Sexual Contact to a *Chlamydia trachomatis* (CT)-Infected Partner Who Tested CT Positive versus Negative by Nucleic Acid Amplification Testing (NAAT)

	Total (N = 73)	CT NAAT Positive (N = 24)	CT NAAT Negative (N = 49)	*P*-value
Age, median (interquartile range [IQR])	22 (20–26)	22 (19–23.5)	23 (21–26)	0.067 *
African American, N (%)	61 (83.6%)	20 (83.3%)	41 (83.7%)	0.607 †
Hispanic, N (%)	1 (1.4%)	0 (0.0%)	1 (2.0%)	0.671 †
Number of sexual partners in last 3 months, median (IQR)	1 (1–2) ††	1 (1–1.5)	1 (1–2)	0.565 *
Number of days from last sexual activity, median (IQR)	7 (3–14)	7 (3–14)	7 (3–17)	0.595 *
Hormonal contraceptive use, N (%)	22 (30.1%)	8 (33.3%)	14 (28.6%)	0.44 †
Reported prior CT infection, N (%)	42 (57.5%)	7 (29.2%)	35 (71.4%)	0.001 †
Asymptomatic, N (%)	36 (49.3%)	11 (45.8%)	25 (51.0%)	0.80 †
Infections at enrollment, N (%)				
Bacterial vaginosis	32 (43.8%)	12 (50%)	20 (40.8%)	0.31 †
Candidiasis	8 (10.9%)	3 (12.5%)	5 (10.2%)	0.526 †
Gonorrhea	6 (8.2%)	3 (12.5%)	3 (6.1%)	0.305 †
Trichomoniasis	8 (10.9%)	4 (16.7%)	4 (8.2%)	0.239 †
Cervicitis, N (%)	5 (6.8%)	5 (20.8%)	0 (0.0%)	0.003 †
Pelvic inflammatory disease, N (%)	1 (1.3%)	0 (0.0%)	1 (2.0%)	0.671 †

*= Wilcoxon rank-sum test;

†= Fisher's exact test

††= missing data for one subject