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MAJOR ARTICLE

Chlamydia Infection Between Men and Women: A Cross-Sectional Study of Heterosexual Partnerships

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Background. Studies of sexual partnerships can further our understanding of the sexual transmission of chlamydia, which is important for informing public health interventions and clinical management. The aim of this study was to ascertain among heterosexual dyads the proportion concordantly infected with chlamydia and factors associated with infection between partners.

Methods. This study was conducted at the Melbourne Sexual Health Centre between January 2006 and March 2015. Heterosexual partners attending the clinic on the same day were identified prospectively. Dyads where 1 or both individuals were diagnosed with chlamydia by a test performed on the day of joint attendance or within the prior 30 days were included. Testing was by strand displacement assay. Men and women with genital symptoms underwent clinical examination.

Results. Of 233 females with chlamydia, 76% (n = 178) of their male partners tested positive. Of the chlamydia-positive females with cervicitis, 91% of males were chlamydia positive. Male infection was less likely if their partner had taken azithromycin or doxycycline within 30 days (7% vs 25%; $P = .039$). Of 235 males with chlamydia, 77% (n = 178) of their female partners tested positive. No associations were found between male symptoms, signs, or recent antibiotic use and a positive chlamydia result in female partners. Sixty-one percent of the dyads were concordantly infected with chlamydia.

Conclusions. These results underscore the high likelihood of heterosexual partners of men and women with chlamydia being infected and the importance that partners are tested and managed appropriately for chlamydia.

Keywords. chlamydia infection; partner notification; sexual health.

Chlamydia trachomatis is the most common sexually transmitted bacterial infection in young men and women. Although most often asymptomatic, untreated chlamydia has potentially serious health impacts in women including pelvic inflammatory disease, ectopic pregnancy, and tubal infertility [1]. The World Health Organization estimated that, in 2012, approximately 130 million people worldwide were infected with chlamydia and that 4.2% of women and 2.7% of men aged 15 to 49 years had a prevalent infection [2]. In Australia, where chlamydia is notifiable, the notification rate of chlamydia in 2015 was 378.8 per 100 000 population [3].

Studies of sexual partnerships can further our understanding of the sexual transmission of chlamydia, which is important for informing public health interventions and clinical management. To date, these studies have been limited to (1) small numbers of partnerships or (2) including partners recruited only after 1 partner has been diagnosed with chlamydia [4–8]. In a study published in 1996, among 101 heterosexual partnerships in which at least 1 partner was polymerase chain reaction (PCR) positive for chlamydia, 52% of dyads were concordantly positive for chlamydia, with female age <20 years and cervical ectopy associated with concordance [7]. In a more recent study, among 128 heterosexual partnerships, concordant chlamydia infection was found in 54.7% of partnerships [8]. The aim of this study was to ascertain among heterosexual men and women, where at least 1 partner had chlamydia, factors associated with partner infection and the proportion of dyads concordantly infected.

METHODS

This study was conducted between January 2006 and March 2015 at the Melbourne Sexual Health Centre, the major public sexually transmitted infection service in Victoria, Australia. During this period, heterosexual partners attending the clinic on the same day were identified prospectively. Individuals attending the clinic were required to undertake a computer-assisted self-interview, which asked whether a sexual partner of the patient was also attending the clinic on the same day, and, if so, the name of this partner. In addition, clinicians recorded the medical record number of the patient's partner in the electronic record of their patient. Male-female sexual partnerships were identified using these data. Individual electronic medical records were reviewed

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to resolve any discrepant information, such as misspelled names, so that sexual partners could be verified. Dyads were included if the following occurred: both individuals attended the clinic on the same day; both were tested for chlamydia; and 1 or both were diagnosed with chlamydia via a test performed either on that day or within the prior 30 days. There were no requirements regarding the duration or exclusivity of the sexual relationship nor the frequency or timing of last sexual contact for sexual partnerships to be included. Dyads were excluded if the male reported sex with any men within the preceding 12 months.

Men attending the clinic were routinely asked by the triage nurse and treating clinician if they had symptoms of urethritis, including dysuria or urethral discharge. Men with these symptoms had a genital examination performed and any urethral discharge noted. Asymptomatic men were not examined. Men were tested for urethral chlamydia using first pass urine. Women attending the clinic were routinely asked whether they had symptoms of possible genital tract infection, including vaginal discharge, irregular vaginal bleeding, or pelvic pain. Women with genital symptoms had a speculum examination of the vagina and cervix and an endocervical swab performed. A diagnosis of cervicitis was made clinically by the treating clinician based on the presence of cervical inflammation, induced cervical bleeding during endocervical swabbing, and/or mucopurulent cervical discharge. Asymptomatic women did not have a speculum examination and were screened for chlamydia using first pass urine or a vaginal swab. Testing was not routinely performed for pharyngeal or rectal chlamydia. Nucleic acid amplification testing (NAAT) for *C trachomatis* was performed on specimens using the BD Probetec strand displacement assay (Becton Dickinson, Franklin Lakes, NJ).

For each individual, data were collected by review of medical records for the following: recent sexual behavior; symptoms and signs associated with lower and upper genital chlamydia infection; azithromycin or doxycycline use within 30 days; and chlamydia test results. Factors associated with partner infection were examined from 2 perspectives: (1) by grouping all females who tested positive, and examining female characteristics associated with infection in their male partners, and (2) by grouping all males who tested positive, and examining male characteristics associated with infection in their female partners. Concordance of infection, ie, the proportion of dyads in which both the male and the female were infected with chlamydia, was determined. Statistical tests included the following: mean and standard deviation for continuous variables; 2-sample *t* test to examine the difference in continuous variables; and the χ^2 test for categorical variables.

In a subset of females, *C trachomatis* organism load was measured using stored specimens. We hypothesized that cervicitis would be associated with transmission to male partners because *C trachomatis* load was higher in women with cervicitis. To test this, we examined the loads of *C trachomatis* in the chlamydia-infected women who had cervicitis on speculum examination and whose partner also tested positive for chlamydia. These were compared with *C trachomatis* loads in chlamydia-infected women who did not have cervicitis on speculum examination and whose partner tested negative for chlamydia. For this substudy, *C trachomatis* detection was determined using a previously described method [9]. The human beta-globin gene was amplified by quantitative PCR (qPCR) using previously described primers [10, 11] and the following TaqMan probe: 6FAM-ACACAACTGTGTTCACTAGC-TAM (PCO3). The chlamydial omp1 and human beta-globin gene load were then determined by comparing the crossing threshold of each sample to the crossing threshold of known quantified controls plotted to form a standard curve. Using beta-globin to (1) standardize across testing at different sites and (2) account for different specimen yields, the results were expressed in copies per 100 human cells (using the assumption of 2 beta-globin genes per cell) and then $\log_{10}$ transformed. Standardizing the loads was also necessary because different specimen types (urine and vaginal swab) were used in the investigation. This study was approved by the Alfred Hospital Research Ethics Committee (Number 417/15).

RESULTS

During the study period, 287 sexual partnerships comprising 287 males and 287 females attended on the same day, and 1 or both individuals within the partnership had chlamydia detected on that day or within the prior 30 days. In addition, there was 1 dyad in which the same 2 individuals presented for separate episodes of care, and 1 man and 1 woman who presented with 2 different partners on separate visits. These 3 presentations were analyzed as separate partnerships, providing a total of 290 dyads for analysis. Fifty-nine percent (n = 170) of dyads attended for their first consultation at the clinic together on the same day. Within the remaining 42% (n = 120) of dyads, 79 females and 51 males had first presented to the clinic a median of 7 days (interquartile range, 6–12) before they attended again with their partner at a joint visit.

The characteristics of the individual men and women within the 290 partnerships are shown in Table 1. Overall, among these dyads, 80% (n = 233) of females and 81% (n = 235) of males tested positive for chlamydia. Compared with males, females were younger, had fewer numbers of sexual partners, and were more likely to present with genital symptoms. The median duration of sexual partnerships was 4 months. Only 5% of dyads reported always using condoms with vaginal sex. In 9% (n = 25) of dyads the male and in 10% (n = 28) of dyads the female had received doxycycline or azithromycin within the previous 30 days.

A total of 178 dyads were concordantly infected with chlamydia (61%; 95% confidence interval, 55%–67%). Concordance was not associated with duration of sexual partnerships. Among the 112 dyads with discordant chlamydia, results were as follows: 55 (49%) cases where only the female tested positive and 57 (51%)

Table 1. Characteristics of Males and Females Within Sexual Partnerships

Characteristics	Men (n = 290)[a]	Women (n = 290)[a]	*P* Value
Mean age (SD)	27.9 (7.6)	25.3 (5.7)	.001[c]
Mean number of sex partners within 3 months (SD)	2.3 (3.6)	1.7 (1.2)	.005[c]
Condom use with vaginal sex			.562
Always	13 (4.5%)	17 (6%)	
Not always	277 (96%)	273 (94%)	
Self-reported history of previous chlamydia infection	46 (16%)	33 (11%)	.116
Received azithromycin or doxycycline within preceding 30 days	25 (9%)	28 (10%)	.187
Presented with potential chlamydia-related symptoms[b]	85 (29%)	108 (37.2%)	.043[c]
Dysuria	65 (22%)	NA	
Urethral discharge	40 (14%)	NA	
Testicular pain	4 (1%)	NA	
Vaginal discharge	NA	72 (25%)	
Abnormal vaginal bleeding	NA	34 (12%)	
Pelvic pain	NA	47 (16%)	
Chlamydia test positive	235 (81%)	233 (80%)	.833
First void urine	235	79	
Cervical swab	NA	124	
Vaginal swab	NA	35	

Abbreviations: NA, not applicable; SD, standard deviation.

[a]The 290 dyads consisted of 287 individual men and 287 individual women. One dyad consisted of the same 2 individuals who had 2 separate episodes of care, 1 man presented with 2 different female partners on separate visits, and 1 woman presented with 2 different male partners on separate visits.

[b]Symptoms considered potentially related to chlamydia were as follows: for men - dysuria, urethral discharge, and testicular pain; for women - vaginal discharge, abnormal vaginal bleeding, and pelvic pain.

[c] denotes statistical significance.

cases where only the male tested positive (Table 2). In women, chlamydia tests were positive in 84% (124 of 147) of cervical, 82% (35 of 43) of vaginal, and 79% (79 of 100) of urine specimens.

Characteristics of the males and females who tested positive for chlamydia were analyzed in relation to whether their partner who also tested positive (Tables 3 and 4). Of the 233 females with chlamydia, 76% (n = 178) of their male sexual partners also tested positive. On univariate analysis, infection in males within these partnerships was significantly associated with their female partner reporting vaginal discharge (28% vs 15%; P = .042) or having cervicitis on physical examination (25% vs 9%; P = .040) (Table 3). Among the 58 females with chlamydia who had vaginal discharge, 50 male partners (86%) were infected whereas 8 (14%) were not infected. Among the 33 females with chlamydia who had cervicitis, 30 males (91%) were infected whereas 3 males (9%) were not infected. Male infection was significantly less likely if the female partner had taken azithromycin or doxycycline within 30 days (7% vs 25%; P = .039) (Table 3). Of the 235 males with chlamydia, 77% (n = 178) of their female partners also tested positive for chlamydia. No associations were found between male symptoms, signs, or recent antibiotic use and a positive chlamydia result in their female partners (Table 4).

Of the 233 women with chlamydia, 153 underwent a speculum examination because they reported genital symptoms, and 33 were diagnosed as having cervicitis. Among the women examined, those with signs of cervicitis were more likely to report vaginal discharge, compared with those who did not have cervicitis (58% vs 31%; P = .005).

For the substudy on chlamydia organism load, stored frozen samples from 26 of the 30 women with cervicitis and 24 of the 31 women without cervicitis were available to test. All samples were beta-globin positive. Of these 50 samples, chlamydia was not detected in 8 samples, 7 of which were from women who did not have cervicitis. There was no significant difference in the mean chlamydia load in women with and without cervicitis: 0.20 of 100 cells ($\log_{10}$) versus 0.43 of 100 cells ($\log_{10}$) (P = .48).

DISCUSSION

To our knowledge, this study, which includes 290 dyads, is the largest study to date that investigates genital chlamydia infection within heterosexual partnerships. We found that 76% of males and 77% of females tested positive for chlamydia by NAAT when their partners tested positive. Infection in males was significantly more likely when their female partner reported vaginal discharge or when their female partner had signs of cervicitis on physical examination. In addition, males were less likely to be infected if their female partner had recently taken azithromycin or doxycycline—for any reason, presumably because treatment prevented transmission between some partners. No factors were identified in males that predicted infection of their female partners.

The rate of concordant chlamydial infection in this study is broadly consistent or somewhat higher than those reported in previous, smaller partner studies [4, 6–8]. Although our finding that male infection was more likely when female partners reported vaginal discharge or had clinical evidence of cervicitis that may be due to more recent transmission to the female, it also led us to hypothesise that women with vaginal discharge and cervicitis may have a higher chlamydia load leading to an increased probability of transmission to their male sexual partners [12]. Higher *C trachomatis* loads in women with vaginal discharge and cervicitis have previously been demonstrated,

Table 2. Chlamydia Results in Male and Females Within Sexual Partnerships[a]

		Female Chlamydia Result		
Chlamydia Result		Positive	Negative	Total
Male Chlamydia result	Positive	178	57	235
	Negative	55	0	55
Total		233	57	290

[a]McNemar's test: P = .925

Table 3. Female Characteristics Associated With Chlamydia Infection in Their Male Partner

Characteristics	Female With Chlamydia (n = 233)	Female With Chlamydia and Male Partner Chlamydia Positive (n = 178)	Female With Chlamydia and Male Partner Chlamydia Negative (n = 55)	*P* Value
Mean age (SD)	25.2 (5.7)	25.0 (5.5)	26.0 (6.5)	.286
Mean number of sex partners within 3 months (SD)	1.7 (1.3)	1.7 (1.2)	1.6 (1.0)	.712
Condom use with vaginal sex				.122
Always	15 (6%)	9 (5%)	6 (11%)	
Not always	218 (94%)	169 (95%)	49 (89%)	
Female received azithromycin or doxycycline within preceding 30 days	27 (12%)	13 (7%)	14 (25%)	.039[a]
Presented with potential chlamydia-related symptoms[b]	90 (39%)	75 (42%)	15 (27%)	.048[a]
Abnormal vaginal bleeding	30 (13%)	23 (13%)	7 (13%)	.970
Pelvic pain	41 (18%)	32 (18%)	9 (16%)	.734
Vaginal discharge	58 (25%)	50 (28%)	8 (15%)	.042[a]
Physical examination findings (n = 153)				
Cervicitis[c]	33 (21%)	30 (25%)	3 (9%)	.040[a]
Pelvic inflammatory disease[c]	41 (18%)	31 (18%)	10 (18%)	.896

Abbreviation: SD, standard deviation.

[a]This *P* value is comparing the male partner chlamydia-positive column with the male partner chlamydia-negative column.

[b]Symptoms considered potentially related to chlamydia were as follows: for women - vaginal discharge, abnormal vaginal bleeding, and pelvic pain.

[c]Cervicitis was determined by the treating clinician based on speculum examination and examination of the cervix. Diagnosis of pelvic inflammatory disease was made by the clinician based on pelvic examination.

particularly in studies using culture-based methods [13]. In a study of 83 dyads, there were higher rates of partner infection when a partner tested positive by culture or direct fluorescent antibody testing compared with infections positive by NAAT alone (75% vs 45%) [4]. It is likely that infections detected by NAAT alone contain lower organism burden than those detected by culture and therefore may be less transmissible. The NAAT may also detect nucleic acid from nonviable organism, including that after treatment, whereas culture requires viable organism. A higher rate of concordant infection with culture-positive compared with NAAT-positive chlamydia was also found in a study by Schillinger et al [8]. In this study, 33.3% of male and 46.4% of female partners of those who tested positive by NAAT only were infected, compared with 78.6% of male and 77% of female partners of those who tested positive by culture. Moreover, Schillinger et al [8] were able to demonstrate

Table 4. Male Characteristics Associated With Chlamydia Infection in Their Female Partner

Characteristics	Male With Chlamydia (n = 235)	Male With Chlamydia and Female Partner Chlamydia Positive (n = 178)	Male With Chlamydia and Female Partner Chlamydia Negative (n = 57)	*P* Value
Mean age (SD)	27.6 (7.2)	27.2 (7.0)	28.7 (7.6)	.173
Mean number of sex partners within 3 months (SD)	2.3 (3.9)	2.3 (3.9)	2.8 (4.2)	.385
Condom use with vaginal sex				.337
Always	11 (5%)	7 (4%)	2 (7%)	
Not always	224 (95%)	171 (96%)	53 (93%)	
Male received azithromycin or doxycycline within preceding 30 days.	19 (8%)	13 (7%)	6 (11%)	.437
Presented with potential chlamydia related symptoms[a]	77 (33%)	58 (33%)	19 (33%)	.916
Dysuria	58 (25%)	45 (25%)	13 (23%)	.706
Urethral discharge	36 (15%)	28 (16%)	8 (14%)	.757
Testicular pain	5 (2%)	3 (2%)	2 (4%)	.406
Physical examination findings (n = 129)				
Urethral discharge	39 (30.2%)	27 (29.7%)	12 (31.6%)	.830
Epididymo-orchitis	4 (3%)	2 (2%)	2 (5%)	.351

Abbreviation: SD, standard deviation.

[a]Symptoms considered potentially related to chlamydia were as follows: for men - dysuria, urethral discharge, and testicular pain.

a significantly higher *C trachomatis* load using qPCR in samples from women with concordant partner infections compared with those whose partners were uninfected. We performed qPCR on samples from a small proportion of participants and did not demonstrate a higher *C trachomatis* load among women with cervicitis. Although we performed beta-globin testing to assess the adequacy of sampling, specimen collection was not standardized, and only small numbers were included, which limited our capacity to accurately explore this question in this cohort. Although it is biologically plausible that higher organism load may be associated with increased transmission risk, other investigators have not consistently found an association between chlamydia load and partner infection [12, 13]. Further research investigating the role of chlamydial organism load and other determinants of chlamydia transmission are warranted.

In a previous study of patients presenting to our clinic who reported sex with a partner with chlamydia, 39.9% of females and 36.1% of heterosexual males tested positive for chlamydia [14]. The comparatively higher rates of chlamydia in the current study may reflect a number of potential factors. First, in this study, chlamydia status was confirmed in each individual at a test taken in the clinic at presentation, whereas in the earlier study, the diagnosis of chlamydia was reported by a sexual partner and not verified. Second, because sexual partners presented together in this study, sexual contact and infection may have been more recent, although the frequency and timing of last sexual contact was not ascertained in this study. We did not find an association between duration of the relationship and chlamydia concordance within dyads. It is notable that the studies by Quinn et al [7] and Schillinger et al [8] did not demonstrate an association between concordance and the number of sexual exposures to an infected partner.

Strengths of this study include the relatively large number of sexual partnerships included, and that the individuals within each dyad were tested contemporaneously. However, our sample may have been biased towards concordant infection if there were factors related to their exposure that made it more likely that both individuals in the partnership would present to the clinic. There are a number of other limitations. First, we could not ascertain the direction of transmission within concordantly infected partners or the probability of transmission per sexual act, limitations inherent to all previous chlamydia partner studies. Uncertainty over the direction of transmission may have reduced the strength of associations between variables examined and infection of partners. Second, we did not perform chlamydia genotyping, and we have assumed that because the sexual partners presented together, they transmitted chlamydia to each other. We cannot exclude other scenarios, for example, where both individuals acquired chlamydia directly from a third person. Schillinger et al [8] found 96.2% genovar concordance within infected sexual partners. However, if there are multiple strains within the same genovar, or common genovars circulating, the same genovar in sexual parthers will not necessarily confirm transmission between individuals. Third, by performing NAAT testing only, we were unable to confirm whether the chlamydia detected was a viable organism capable of transmission or establishing infection. Finally, the sensitivity of chlamydia detection is influenced by the sample type, adequacy of sampling, and the performance of the particular diagnostic assay [15]. Although the diagnostic assay used throughout the period remained the same, specimen collection was not standardized because tests were performed as part of routine clinical care.

CONCLUSIONS

This study contributes additional data for the concordance of chlamydia within heterosexual partnerships, which helps improve the precision of the estimate for this parameter for mathematical modeling of chlamydia transmission. Furthermore, the findings underscore the high likelihood of sexual partners of individuals with chlamydia being infected and therefore the importance of testing and appropriate management of the sexual partners of heterosexual men and women diagnosed with chlamydia.

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All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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