Generation C: Prevalence of and Risk Factors for *Chlamydia trachomatis* among Adolescents and Young Women in Lima, Peru

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Abstract

Objective: Adolescent and young adult women in urban, socioeconomically disadvantaged areas are at high risk of contracting sexually transmitted infections (STIs). We assessed associations of *Chlamydia trachomatis* (CT) infection with both traditional STI risk factors, and partner and partnership-related factors among low-income women in Lima, Peru, by age group.

Methods: In a cross-sectional analysis of CT infection among 1290 postpartum women, cervical swabs were collected for CT polymerase chain reaction (PCR) within 48 h after delivery, and a structured interview was completed. Multivariate logistic regression was used to evaluate risk factors for CT, with separate models stratified by age: adolescents (12–19 years), young women (20–24 years), and older women (≥ 25 years).

Results: CT was detected in 9.6% of adolescents, 9.0% of young women, and 5.4% of older women ($p = 0.03$). Among adolescents, history of drug use (odds ratio [OR] = 5.62, 95% confidence interval [CI] 1.03–30.6) and short duration of current partnership (OR = 2.6, 95% CI 1.14–5.93) were the strongest predictors of CT infection. Among young women, younger age at coitarche (OR = 0.74 for each year older, 95% CI 0.60–0.91) and low income (OR = 2.40, 95% CI 1.04–5.55) were associated with CT, while self-report of ever using condoms was protective (OR = 0.22, 95% CI 0.08–0.61). Among older women, only younger age at coitarche was related to CT (OR = 0.85, 95% CI 0.75–0.97).

Conclusions: Risk factors for CT among women in Lima, Peru, differed for adolescents, young women, and older women, which may reflect differences in biology and/or immunology of CT as well as variability in the occurrence of specific risk behaviors by age group.

Introduction

GLOBALLY, *Chlamydia trachomatis* (CT) is the most common bacterial sexually transmitted infection (STI) and disproportionately affects women, resulting in a significant burden of lifelong reproductive morbidity.¹ Among pregnant women, CT infection is associated with increased risk of adverse reproductive outcomes, including preterm birth and low birth weight.^{2,3} If untreated, chronic CT infection can lead to serious upper reproductive tract sequelae, including pelvic inflammatory disease and infertility,⁴ and may increase the risk of transmission of human immunodeficiency virus (HIV).^{5,6} Diagnosis and treatment are often delayed or com-

plicated by the fact that infection is asymptomatic in a majority of women.⁷

The epidemiology of CT infection mirrors that of most other STIs, with common risk factors, including behaviors like young age at sexual debut, multiple partners, and inconsistent condom use as well as socioeconomic factors. While it is well established that adolescent girls and young women under 25 years of age have the highest prevalence of CT infection,^{8,9} the reasons for this are not entirely clear. It may simply be that adolescents and young women have a higher frequency of STI risk factors, but there also could be important differences in biological or immunological susceptibility to CT infection by age.⁸

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Adolescents and younger women also may be more likely to have partners who engage in high-risk behaviors. While a woman's own high-risk behaviors are commonly ascertained in STI research, those of her partner(s) are less frequently considered. However, partner and partnership-related factors may be equally important determinants of STI acquisition for women, especially in populations where women engage in few risk behaviors themselves. Recent studies in Peru^{10,11} and elsewhere^{12,13} suggest that partner behavior may be a strong predictor of HIV and other STI risk in women.

The objective of this study was to investigate whether behavioral risk factors for CT infection (including partner/partnership characteristics) vary by age. We hypothesized that the risk of CT in adolescents might be strongly related to partner risk factors, whereas CT among older women might be driven more by personal risk factors.

Methods

This cross-sectional analysis was based on data from a case-control study investigating infectious causes of preterm birth. The study was conducted at the Instituto Nacional Materno Perinatal (INMP) in Lima, Peru, between October 2002 and June 2004. This large maternity hospital serves a primarily low-income, urban population, averaging 20,000 deliveries per year (15% of all deliveries in Lima). Potential subjects were screened for eligibility immediately after delivery. Preterm cases included women with a spontaneous preterm delivery at 20–36 weeks' gestation, and term controls included the next consecutive spontaneous term delivery (at ≥ 37 weeks' gestation) after each preterm case, with a case/control ratio of 1:1. All women provided written informed consent, and the study was approved by the INMP and University of Washington Institutional Review Boards.

Within 48 hours after delivery, women underwent a structured interview conducted in Spanish with collection of demographic, reproductive, medical, and behavioral data, including the woman's assessment of her partner's behavioral risk factors for STI. Given the sensitive nature of some questions, special care was taken to ensure subject privacy and confidentiality and to encourage accurate reporting of potentially socially undesirable behaviors. A separate page of the interview questionnaire ascertaining sensitive information, including sexual behavior and partner/partnership-related factors, was completed by the woman herself with no interviewer present, and was placed in a sealed envelope and deposited in a box. Women were assured that all of their answers would remain anonymous and would be available only to authorized study personnel.

A pelvic examination was performed using a sterile, unlubricated speculum. The cervix was visualized and lochia removed using large cotton-tipped swabs. A Dacron swab was obtained from the endocervix for *C. trachomatis* and *N. gonorrhoeae* PCR (AMPLICOR, Roche Diagnostics); the swab was placed in a sterile cryovial containing 2M-sucrose-phosphate transport medium, immediately placed on dry ice, and then stored at -70°C until assayed.

All partner and partnership factors were dichotomous (yes/no or ever/never) based on the original interview questionnaire, or were dichotomized at a relevant threshold for analysis (paternal-maternal age difference, categorized as >5 years or not, and short duration with current partner, cate-

gorized as <2 years or not). Partnership characteristics, including paternal-maternal age difference and duration of relationship, were necessarily specific to the current partner, as were factors including perception of one's partner as a womanizer ("mujeriego") and belief that one's partner visited prostitutes. In contrast, questions relating to history of anal sex, partner drug use, and partner prison history asked about any current or previous partner. Concurrency was defined dichotomously based on a woman's answer to the question: "Have you ever had occasional partners at the same time as your regular partner?" Women were also asked about the reason(s) they used condoms (contraception, STD protection, both, or never used condoms); for the purposes of analysis, this variable was re-categorized as ever used condoms (for any purpose) or never used condoms.

Statistical analysis

Statistical analyses were conducted using Stata 9.2 (Stata-Corp, College Station, TX). Both the overall and age-specific prevalence of CT were calculated. Age groups were chosen based on the *a priori* hypothesis that adolescents and young adults might show different risk factors for CT. Univariate descriptive analyses were conducted to evaluate crude associations and potential confounders; chi-squared and Fisher's exact tests were used for categorical variables, while Student's *t*-tests and non-parametric Mann-Whitney *U*-tests were used for continuous variables. Logistic regression was used to evaluate multivariate associations with CT, stratified by age group (adolescents ≤ 19 years, young women 20–24 years, women 25+ years). Variables were retained in the multivariate models if they were established risk factors based on prior literature or if they approached statistical significance ($p < 0.10$) in univariate analyses. The same set of predictor variables was retained in each model for parsimony, regardless of whether each variable was statistically significant in every age group. Because of their close relationship, variables measuring partner concurrency and condom use were always retained together in multivariate models.

Results

Of 1336 women enrolled, a total of 1290 (97%) with complete data on CT status, demographic, behavioral, and reproductive history, and partner/partnership-related factors were included in this analysis. The average age was 24.6 ± 6.8 years (range, 12–47 years), and average monthly household income was US \$138 $\pm$ 62. The majority were married or living with a partner (75%), had a high school education or higher (86%), and slightly more than half had just delivered their first child (52%); 42% of women were immigrants to Lima from other areas of Peru (data not shown).

Overall, 98 women tested positive for CT (7.6%). The age-specific CT prevalence decreased from a high of 10.9% in girls aged 12–15 years to a low of 3.1% in women 35 years and older (Fig. 1). Women with CT infection were younger (22.6 vs. 24.7 years, $p = 0.001$), had lower household incomes (US\$131 vs. \$139, $p = 0.13$), and were slightly more likely to be single (32% vs. 23%, $p = 0.13$) than women without CT. Those with CT were more likely to report a history of illegal drug use (5% vs. 2%, $p = 0.013$), less than 2 years with current partner (41% vs. 27%, $p = 0.003$), younger age at sexual debut (16.5 vs. 17.8 years, $p < 0.001$), and a higher lifetime number of sexual

FIG. 1. Prevalence of CT infection by age group (years). n = total number of women in each age group.

partners (1.74 vs. 1.58, $p = 0.10$), and were less likely to report ever having used condoms (31% vs. 44%, $p = 0.011$; Table 1). CT infection was not associated with preterm birth case/control status in the parent study ($p = 0.77$). Only one woman tested positive for *N. gonorrhoeae* infection.

In the stratified multivariate logistic models, for adolescents (Table 2), only a history of illegal drug use (adjusted odds ratio [aOR] = 5.62, 95% CI 1.03–30.6) and short duration of current partnership (aOR = 5.62, 95% CI 1.14–5.93) were independently associated with CT infection; the effect of reporting having ever used condoms was protective, although not significantly so (aOR = 0.44, 95% CI 0.17–1.14). Among young adult women (20–24 years), having a low income (aOR = 2.40, 95% CI 1.04–5.55) and younger age at first intercourse (aOR = 0.74, 95% CI 0.60–0.91) were significantly associated with CT infection, while condom use was strongly protective (aOR = 0.22, 95% CI 0.08–0.61). While it did not reach statistical significance, there was some evidence among adolescents and young adult women of an association between having ever had a concurrent relationship and CT infection. Among older women, the only significant predictor of CT infection was younger age at coitarche (aOR = 0.85, 95% CI 0.75–0.97).

Discussion

The overall prevalence of CT infection in this population of women delivering in a Lima maternity hospital was 7.6%, similar to the global median estimate of 8% among low-risk pregnant women in developing countries.¹⁴ Consistent with prior studies, we observed the highest prevalence of CT infection in the youngest adolescents. The high prevalence of CT in younger age groups may be due to increased biologic and/or immunologic susceptibility to acquiring infection per infectious contact. Adolescent girls and young women do not yet have fully mature reproductive and immune systems, so they may be unable to mount a strong defense against infection;¹⁵ specifically, they are more likely to have cervical ectopy, which has been shown to be associated with CT across most studies.^{7,16–19} Ectopy is thought to increase the risk of

infection by allowing exposure of more susceptible columnar epithelial cells.

In addition to biologic considerations, there may also be social and contextual factors that broadly increase the vulnerability of this age group to CT infection. As a result of gender roles and differences in normative sexual and reproductive behavior, early sexual experiences for adolescent girls and young women in many cultures may be especially subject to coercion.⁸ Overall, younger women are less likely to have complete control over their own sexual choices and are less able than more mature women to negotiate protective behaviors like condom use with their partners. The high prevalence of CT may also be related to inadequate access to health care and/or poor treatment-seeking behavior in this age group,¹⁵ which may lead to delays in treatment and a longer duration of infectiousness.

The strongest predictors of CT infection differed importantly by age group in this population. Specifically, traditional STI risk factors like younger age at sexual debut and multiple sexual partners were not associated with CT infection among adolescents 12–19 years old, which could suggest that a broader set of risk factors must be considered in this age group. The strongest predictors of CT infection among adolescent girls were non-specific markers of risk: history of drug use and short duration of current partnership. Among young adult women aged 20–24, having a low income was significantly associated with CT even after adjustment for behavioral STI risk factors, raising the possibility of transactional sex in this age group. Condom use ever was associated with lower CT prevalence in all age groups, although this result was only statistically significant for women 20–24 years old. The distribution of various other risk factors differs by age, but the strength and direction of the associations with CT also appear to differ by age. Overall, these observations suggest that adolescents and young women represent uniquely vulnerable populations at risk of STIs and may require different prevention and treatment interventions.

A growing body of literature suggests that in many settings, a woman's risk of acquiring HIV or other STIs may be more dependent on her partner's risk behaviors

TABLE 1. DEMOGRAPHIC, BEHAVIORAL, AND PARTNER/PARTNERSHIP CHARACTERISTICS OF THE STUDY POPULATION, STRATIFIED BY CT INFECTION STATUS

	CT positive, N = 98	CT negative, N = 1,192	p
Age (years)	22.6 ± 5.8	24.7 ± 6.9	0.001
Education			
Illiterate	0 (0)	7 (<1)	0.62
Primary school	13 (13)	159 (13)	
High school	77 (79)	871 (73)	
Technical/college	8 (8)	155 (13)	
Marital status			
Single	31 (32)	276 (23)	0.13
Married/living together	65 (66)	906 (76)	
Separated/divorced	2 (2)	10 (1)	
Parity			
Primiparous	54 (55)	695 (58)	0.54
Multiparous	44 (45)	497 (42)	
Immigrant to Lima	45 (46)	488 (41)	0.34
Household income (US\$)	\$131 ± 50	\$139 ± 63	0.13
Low income ^a	55 (58)	561 (48)	0.08
Age at coitarche (years)	16.5 ± 2.3	17.8 ± 3.4	<0.001
Lifetime no. of partners	1.74 ± 1.0	1.58 ± 0.8	0.10
History of STD	3 (3)	65 (5)	0.31
History of illegal drug use	5 (5)	19 (2)	0.013
Cigarette smoking ^b	7 (7)	73 (6)	0.67
Alcohol use ^b	20 (21)	224 (19)	0.67
Condom use (ever)	30 (31)	522 (44)	0.011
Partner drug history	7 (7)	95 (8)	0.77
Partner prison history	4 (4)	30 (3)	0.34
Anal sex with any partner	23 (23)	301 (25)	0.69
Partner perceived as “womanizer”	31 (32)	299 (25)	0.17
Partner visits prostitutes	14 (14)	199 (17)	0.54
Large age difference ^c	28 (29)	312 (26)	0.55
Short duration with current partner (<2 years)	40 (41)	319 (27)	0.003

^aMonthly household income less than the median value in the study population.

^bDuring pregnancy.

^cPaternal-maternal age difference greater than five years.

Data are presented as mean ± SD for continuous variables and *n* (%) for categorical variables.

CT, *Chlamydia trachomatis*.

TABLE 2. MULTIVARIATE LOGISTIC MODEL, BY AGE GROUP

	Age <19 years, N = 363, OR (95% CI)	Age 20–24 years, N = 356, OR (95% CI)	Age 25+ years, N = 571, OR (95% CI)
Low income ^c	1.26 (0.59–2.71)	2.40 (1.04–5.55) ^a	1.02 (0.49–2.15)
Age at coitarche	1.14 (0.89–1.45)	0.74 (0.60–0.91) ^b	0.85 (0.75–0.97) ^a
Lifetime partners	0.90 (0.50–1.60)	1.37 (0.88–2.13)	1.08 (0.67–1.76)
History of illegal drug use	5.62 (1.03–30.6) ^a	N/A ^d	2.27 (0.24–21.5)
Ever concurrency	2.92 (0.64–13.2)	2.12 (0.45–10.0)	0.43 (0.05–3.51)
Ever condom use	0.44 (0.17–1.14)	0.22 (0.08–0.61) ^b	0.71 (0.33–1.52)
Partner is “womanizer”	1.43 (0.64–3.19)	1.00 (0.41–2.44)	0.78 (0.33–1.81)
Short duration with current partner (<2 years)	2.60 (1.14–5.93) ^a	1.80 (0.73–4.43)	0.57 (0.13–2.58)

^a*p* < 0.05.

^b*p* < 0.01.

^cMonthly household income less than the study median.

^dOR cannot be calculated due to zero values in one or more cells.

Analyses simultaneously adjusted for all variables in table.

OR, odds ratio; CI, confidence interval.

than her own. A clinic-based survey of sexual behavior and STI antibodies conducted in Lima in the early 1990s observed that, while most risk behaviors, including number of partners were much higher for men than women, the frequency of STI seropositivity was consistently higher in women,²⁰ strongly implying that risky behavior among Peruvian men in part drives STI rates in Peruvian women. In an analysis of pregnant women seeking care at the INMP in Lima, partner and partnership-related factors (perception of partner as a "womanizer," partner history of illegal drug use) reported by a woman were strongly related to her HIV serostatus, independent of her own risk behaviors.¹⁰ Another recent case-control study of HIV+ and HIV- women in Peru observed that partner risk behaviors, including sex with female sex workers (FSWs) or sex with other men, were the strongest predictors of HIV status, and that even monogamous women had extraordinarily large sexual networks due to partner behavior.¹¹

However, with the possible exception of short duration of current partnership, and ever using condoms, our results did not elucidate other partner and partnership-related factors associated with CT infection in this population. The interview questions in this study may not have ascertained the most relevant partner and partnership-related factors with respect to CT infection, and it may be that the best partnership predictors vary by infection (i.e., partner factors related to HIV risk may be different than those related to CT risk). Future research will be needed to identify what specific types of partner and partnership information are most important to collect in STI studies, determine the discrete domains they represent and mechanisms through which they may act, and eventually to develop and validate appropriate survey instruments to ascertain such data.

Because this study took place in a maternity hospital and enrolled a large number of women antenatally, estimates of prevalence and risk factors for CT are likely to be representative of the general population of low-income pregnant women in Lima. This is a major strength in comparison to studies conducted in STI clinics or other high-risk groups where women may be specifically seeking care for genital tract symptoms. We did not observe any association between CT infection and preterm birth in this study population, so it is unlikely that CT prevalence was overestimated due to the case-control design of the parent study. While hospital recruitment may sometimes be considered a limitation in terms of generalizability, the vast majority of women in Lima deliver in a hospital setting as opposed to at home.

There are several important limitations to this analysis. First, given the cross-sectional study design, we are not able to infer causality. Studies that prospectively ascertain new infections will more conclusively demonstrate temporal relationships of risk factors to acquisition of CT. Second, the study was not originally powered for stratified analysis, and there may not have been adequate power to detect modest effects within each age stratum. Lastly, calendar age and age at sexual debut were positively correlated in this population (i.e., younger women reported a younger age of coitarche on average), making it very difficult to separate the effects of these two factors. Thus, we chose to stratify all multivariate analyses by age group in order to be able to evaluate the independent effect of age at coitarche, but this eliminated our ability to evaluate the effect of age directly. This choice also

complicates interpretation and comparison of some variables across age groups, in that adolescents and younger women have had less opportunity for many exposures that may accumulate over the lifetime.

Conclusions

Young, parous women in Lima, Peru, have a very high burden of undiagnosed CT infection, a finding that may have both biological and behavioral explanations. Since the strongest predictors of CT infection appear to differ for adolescents and young women compared to older women, new age-specific prevention programs could be further explored to proactively address this epidemic and prevent future reproductive morbidity.

Screening and treatment for CT is not currently the standard of care for pregnant women in Peru. The high prevalence of undiagnosed CT infection we observed in this population is very concerning, especially given that the majority of women did present for prenatal care prior to delivery. This suggests that pregnant women and their infants could benefit significantly from CT screening and treatment as a routine component of prenatal care in Peru.

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Disclosure Statement

No competing financial interests exist.

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