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High Prevalence of Extra-Genital *Chlamydia* and *Gonorrhoeae* Infection Among Men who have Sex with Men and Transgender-Women in Lima, Peru

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Introduction

Chlamydia trachomatis and *Neisseria gonorrhoeae* infections are among the most common bacterial sexually transmitted infections (STIs) in the world.¹ In Peru, among men who have sex with men (MSM) the prevalence of urethral *N. gonorrhoeae* and/or *C. trachomatis* infections has been shown to be as high as 5.5%,² but data regarding extra-genital infections are sparse. To our knowledge only one other study has characterized this disease burden, but in a non-clinic-based population. That study found a prevalence of anal and pharyngeal *C. trachomatis* infection of 19.0% and 4.8%, respectively, as well as anal and pharyngeal *N. gonorrhoeae* infection of 9.6% and 6.5%, respectively, among MSM and transgender women in Lima, Peru.³ The lack of published data may be because traditional screening methods are based on urethral swabs and urine specimens, which do not detect extra-genital infections. Previous studies in the United States have shown that more than 70% of extra-genital *N. gonorrhoeae* infections, and more than 85% of extra-genital *C. trachomatis* infections were associated with a negative urethral test at the same visit.⁴ Additionally, screening efforts for extra-genital infections have been noted to be far less than for urethral infections.⁴

Accurate detection and treatment of extra-genital infection will reduce further transmission as well as associated economic and social impacts of the disease.^{5]} The present study aims to characterize the disease burden of extra-genital *C. trachomatis* and *N. gonorrhoeae*

Declaration of conflicting interests

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infections, as well as to identify risk factors for infection, among MSM and transgender women in Lima, Peru, in order to better inform screening efforts.

Methods

This cross-sectional analysis was conducted using baseline data from participants in a cohort study in Lima, Peru between May 2013 and May 2014.⁶ The study sample on which the cross-sectional analysis was performed consisted of members of the cohort, and included MSM and transgender women presenting for care or testing at one of two sexual health clinics in Lima, Peru. Alberto Barton Clinic is a municipal clinic for sexually transmitted infections (STIs) and HIV infection, publicly funded and staffed in Callao, a port city adjacent Lima, Peru. Epicentro is a gay men's community center and health clinic. Both provide no or very low cost services. Cohort study participants included men who have sex with men or male-to-female transgender women, at least 18 years of age, willing to participate in study procedures, living in Lima with plans to remain, and agreed to provide informed consent. Additionally, since one of the main purposes of the overall study was to investigate syphilis and repeat syphilis infections, to be eligible to join the cohort participants had to have at least three of the following: a positive syphilis rapid test, a positive HIV rapid test, five or more years of sexual activity, five or more sex partners in the past three months, diagnosed with a STD within the last six months, currently reporting an ulcerative STD, or reporting five or more episodes of condomless receptive anal intercourse with a male partner in the past six months.

A structured interview was conducted with each participant by a trained counselor that included questions about sex and gender identity (as reported by each participants), sexual role, alcohol use prior to sexual intercourse, number of male partners in the last three months, history of exchanging money for sex in the prior three months, the use of condoms, and about unmet basic needs (lack of adequate water, food, or shelter, and for how many months in the previous year).

Patients were instructed in proper self-collection of anal swabs, which, in addition to staff-collected pharyngeal swab specimens, were tested using the Aptima Combo 2 for *C. trachomatis*/N. gonorrhoeae assay (Hologic, San Diego, CA, USA). Because the frequency of asymptomatic urethral infection in males is low (some studies indicating less than 1%),⁷ we decided not to routinely screen participants for asymptomatic urethral infection. Participants found to be infected were treated according to Peruvian national guidelines.⁸

Descriptive statistics were used to summarize socio-demographic characteristics and reported behaviors. Bivariate statistics included calculation of prevalence ratios, which were used to examine the association between anal or pharyngeal infections with socio-demographic characteristics and sexual risk behaviors. Multivariate modeling was performed using a full model approach where all variables that had a *p* value < 0.1 in the bivariate analysis were included in the final model, and adjusted prevalence ratios were reported. Variables accounted for in calculating the adjusted prevalence ratio of anal infections include age, sex role for anal sex, and use of any antibiotic in the past three months. Variables accounted for in calculating the adjusted prevalence ratio of pharyngeal infections include

age and sex/gender identity. All analyses were conducted using STATA software version 13 (College Station, TX, USA). Funding for this study came from National Institutes of Health (NIH)/National Institute of Allergy and Infectious Diseases (NIAID): 1R01AI099727. Ethical approval for this study was granted by the Ethics Committee at Universidad Peruana Cayetano Heredia with written and informed consent obtained from all patients. UCLA determined that the analysis of de-identified data were exempt from ethical review.

Results

The study sample included 298 MSM and 85 transgender women four participants declined to answer regarding sex/gender identity. The median age of the sample was 29.6 years (interquartile range 23.7–38.4), with an average number of male sex partners of five (interquartile range 2–10) in the past three months. Of the 387 participants, 212 (54.8%) reported a sex identity of gay, and 86 (22.2%) reported bisexual/heterosexual identity. Additionally, of the 387 participants, 205 (53.0%) reported having condomless receptive anal intercourse with a male partner in the past three months. The sample included 116 (30.0%) that reported a history of exchange of sex for money in the past three months.

Overall, 127 (32.8%) participants had anal or pharyngeal *C. trachomatis* or *N. gonorrhoeae* infections. Fifty-three (13.7%) had anal infections with *C. trachomatis*, while 34 (8.8%) had anal infections with *N. gonorrhoeae*. Twenty-two (5.7%) participants had pharyngeal infection with *C. trachomatis*, whereas 25 (6.5%) had pharyngeal infections with *N. gonorrhoeae* (Figure).

Discussion

This study demonstrates that the prevalence of extra-genital *C. trachomatis* or *N. gonorrhoeae* infection is considerable among this sample of MSM and transgender women in Lima, Peru. A similarly high burden of infection and associated high incidence was recently reported in a community sample of MSM and transgender women in Lima by Leon et al.³ Explanations for the high rates of infection among MSM and transgender women may be due to a lack of routine screening efforts for extra-genital infections, poor access to STI treatment services, and high rates of sexual risk behaviors.

Other studies have reported risk factors for anal *C. trachomatis* infections including practicing condomless receptive anal intercourse, and reporting greater numbers of casual sex partners.^{9,10} Our analysis showed that practicing both receptive and insertive anal intercourse was associated with extra-genital infections in this high-risk population, but we did not find an association between extra-genital infections and the number of sex partners reported. That finding may be because our study population was an inherently high-risk population, in which there were little variance in the number of sexual contacts. Additionally, we found the prevalence of anal *C. trachomatis* or *N. gonorrhoeae* infection was lower in participants who had used antibiotics in the past three months, which may be due to inadvertent treatment of an undiagnosed infection. A previous study has shown that doxycycline prophylaxis can reduce the incidence of *N. gonorrhoeae* and *C. trachomatis* infection.¹¹ Our findings are also in agreement with previous studies, demonstrating that

younger age is associated with higher incidence of anal *N. gonorrhoeae* and *C. trachomatis* infection,^{9,10} possibly because younger populations have greater number of sexual contacts, as well as a higher likelihood of infection among those contacts. Pharyngeal *C. trachomatis* and *N. gonorrhoeae* infection have also been shown to be associated with receptive oral intercourse.¹²

Previous studies have shown that a history of two prior rectal infections of either *C. trachomatis* or *N. gonorrhoeae* is associated with an eightfold increase in the incidence of HIV infection.¹³ It has been hypothesized that that association is due to risk factors common for HIV and anal *C. trachomatis* and *N. gonorrhoeae* infections,¹⁰ as well as increased biologic susceptibility due to increased cytokine and other inflammatory markers that modulate cell receptors and innate immunity.¹⁴⁻¹⁶ Additionally, drug resistant *N. gonorrhoeae* has been shown to be higher in pharyngeal reservoirs,¹⁷⁻¹⁹ and thus there is concern that pharyngeal infections might perhaps serve to promote resistance by facilitating transformation through the transfer of genetic elements between commensal *Neisseria* species and *N. gonorrhoeae* in the pharynx of an infected host.¹⁸ Therefore, screening and treatment for extra-genital infections with *C. trachomatis* and *N. gonorrhoeae* among populations at risk may reduce the incidence of HIV infections and antibiotic resistance, as well as lower the transmission rates of such infections and reduce the overall disease burden.

Currently Peru has no national guidelines specifically recommending extra-genital STI screening. Recent guidelines, however, have been released by the World Health Organization, which includes periodic screening for urethral and anal *C. trachomatis* and *N. gonorrhoeae* infections as part of the essential STIs package.²⁰ Our findings might inform the next revision of the Peruvian STI treatment guidelines to include routine screening for extra-genital *C. trachomatis* and *N. gonorrhoeae* infections in high-risk groups.

Important to consider in interpretation of the results of the present study is the difference between heterosexually or bisexually identified men who have sex with men and transgender women. Among transgender women we found higher rates of pharyngeal infection compared to MSM, however, there was no difference between rates of anal infections. Other studies have also found such differences. In Los Angeles, for example, one study demonstrated higher rates of homelessness as well as lower levels of education among transgender women compared to MSM, factors which have been previously associated with increased rates of STIs.²¹ The sample size in the present study was not large enough for rigorous between-group analyses, and additional research is needed to further characterize precise differences between MSM and transgender women and the risk for extra-genital STIs.

Limitations

One important limitation of this study is that it was done exclusively in a high-risk cohort; therefore the results are not generalizable to the larger population of MSM or transgender women in Lima, Peru, or even those routinely presenting to sexual health clinics in Lima. Additionally, urethral swabs or urine specimens were not collected, so associations between extra-genital and urogenital infections could not be determined. However, the aim of this

study was to characterize the burden of infection within this high-risk population, which is not dependent on generalizability nor on association with urogenital infections, and thus the results of this study are still valid.

Conclusion

We found there to be a considerable burden of extra-genital *C. trachomatis* and *N. gonorrhoeae* infections among high-risk MSM and transgender women in Lima, Peru. Screening programs for extra-genital *C. trachomatis* and *N. gonorrhoeae* infection should be considered. Further research is necessary to understand the most optimal and cost-effective screening and treatment strategies.

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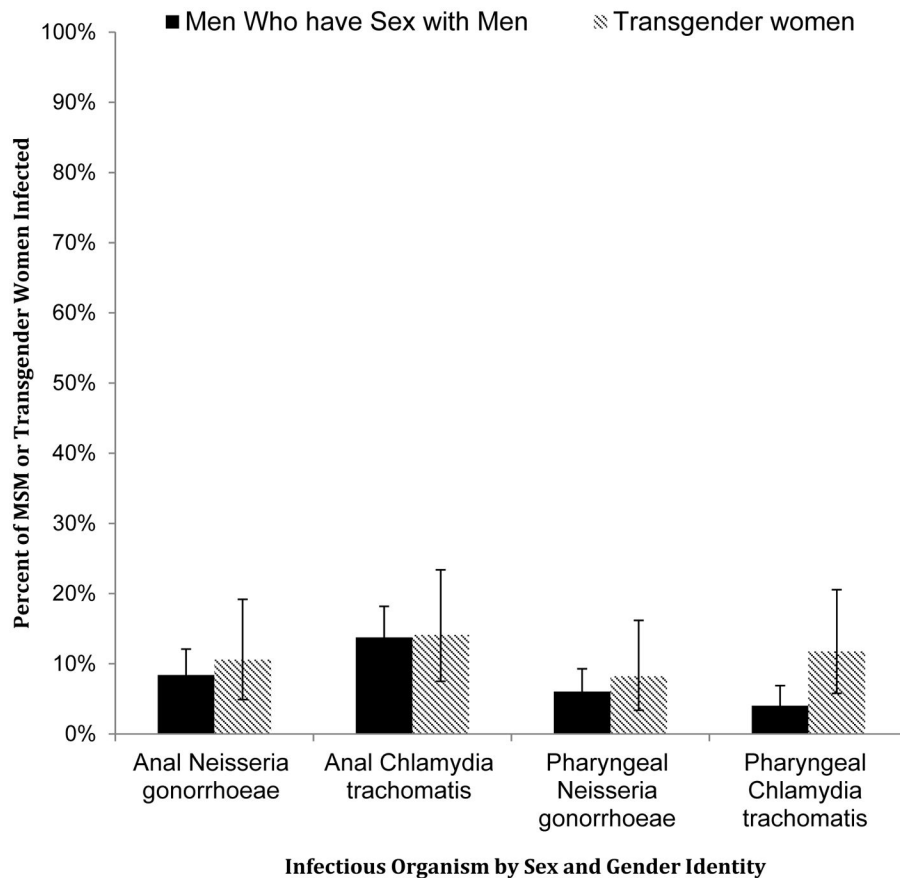


Figure 1.

Percent of men who have sex with men or transgender women infected with either anal or pharyngeal *Neisseria gonorrhoeae* or *Chlamydia trachomatis* from a clinic-based cohort in Lima, Peru between May 2013 and May 2014.

MSM: men who have sex with men.

Anal infection with *N. gonorrhoeae* or *C. trachomatis* was positively associated with practicing both receptive and insertive anal sex, when compared to insertive only (adjusted PR = 2.49; 95% CI = 1.32–4.71), and negatively associated with antibiotic use in the prior three months compared to those with no reported antibiotic use (adjusted PR = 0.60; 95% CI = 0.39–0.91). Pharyngeal infection with *N. gonorrhoeae* or *C. trachomatis* was negatively associated with age older than 30 years when compared to age between 18 and 30 years (adjusted PR = 0.54; 95% CI = 0.30–0.96), and positively associated with gender identity of transgender women (adjusted PR = 2.12; 95% CI = 1.20–3.73) (Table).

Table 1

Risk Factors for Pharyngeal and Anal Chlamydial or Gonococcal Infections Among a Clinic-Based Cohort of Men who have Sex with Men and Transgender Women from Lima, Peru between May 2013–May 2014

	Number of Participants with Anal Infection	Prevalence of Anal <i>Chlamydia trachomatis</i> or <i>Neisseria gonorrhoeae</i> Infections	Crude PR	CI	Adjusted PR	CI	Number of Participants with Pharyngeal Infection	Prevalence of Pharyngeal <i>Chlamydia trachomatis</i> or <i>Neisseria gonorrhoeae</i> Infections	Crude PR	CI	Adjusted PR	CI
Overall	82/387	21%					45/387	12%				
Age (years)												
18–30	50/201	25%	Ref		Ref		29/201	14%	Ref		Ref	
30+	32/186	17%	0.69	0.47 – 1.02	0.70	0.47 – 1.02	16/186	9%	0.59	0.33 – 1.06	0.54	0.30 – 0.97
Unmet basic needs (months, last year)												
0	31/150	21%	Ref				21/150	14%	Ref			
1–3	27/116	23%	1.13	0.71 – 1.78			10/116	9%	0.62	0.30 – 1.26		
4–12	24/121	20%	0.96	0.60 – 1.55			14/121	12%	0.83	0.44 – 1.56		
Sex identity / Gender Identity*												
MSM	61/298	20%	Ref				29/298	10%	Ref		Ref	
Transgender	19/85	22%	1.09	0.69 – 1.72			16/85	19%	1.93	1.10 – 3.39	2.12	1.20 – 3.73
Sex role for anal sex												
Insertive	10/87	11%	Ref		Ref		7/87	8%	Ref			
Receptive	24/123	20%	1.7	0.86 – 3.37	1.74	0.87 – 3.48	15/123	12%	1.52	0.64 – 3.56		
Both Insertive and Receptive	48/177	27%	2.36	1.25 – 4.44	2.49	1.32 – 4.71	23/177	13%	1.62	0.72 – 3.62		
Used any antibiotic in past 3 months*												
No	56/229	24%	Ref		Ref		23/229	10%	Ref			
Yes	25/157	16%	0.65	0.43 – 0.99	0.6	0.39 – 0.91	22/157	14%	1.4	0.81 – 2.42		

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	Number of Participants with Anal Infection	Prevalence of Anal <i>Chlamydia trachomatis</i> or <i>Neisseria gonorrhoeae</i> Infections	Crude PR	CI	Adjusted PR	CI	Number of Participants with Pharyngeal Infection	Prevalence of Pharyngeal <i>Chlamydia trachomatis</i> or <i>Neisseria gonorrhoeae</i> Infections	Crude PR	CI	Adjusted PR	CI
Used any alcohol before last sexual encounter*												
No	58/267	22%	Ref				29/267	11%	Ref			
Yes	24/120	20%	0.92	0.60 – 1.41			2/15	13%	1.23	0.69 – 2.17		
Number of male sex partners in the past 3 months												
0 – 2	26/117	22%	Ref				13/117	11%	Ref			
3 – 5	25/112	22%	1	0.62 – 1.63			16/112	14%	1.29	0.65 – 2.55		
6 – 10	14/65	22%	0.97	0.55 – 1.72			5/65	8%	0.69	0.26 – 1.86		
11+	17/93	18%	0.82	0.48 – 1.42			11/93	12%	1.06	0.50 – 2.27		
Had condomless receptive sex with a male partner in the past 3 months**												
No	32/178	18%	Ref				14/116	12%	Ref			
Yes	50/205	24%	1.36	0.91 – 2.02			31/267	12%	0.96	0.53 – 1.74		
History of exchanging money for sex in past 3 months												
No	61/271	23%	Ref				28/271	10%	Ref			
Yes	21/116	18%	0.8	0.51 – 1.26			17/116	15%	1.42	0.81 – 2.49		

* Has missing values

† For pharyngeal infections, this variable refers to performing condomless fellatio with a male partner in the past 3 months, however for anal infections this variable refers to having condomless receptive anal sex with a male partner in the past 3 months

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For anal infections, variables accounted for in calculating adjusted prevalence ratios include Age, Sex role for anal sex, and Use of any antibiotic in the past 3 months

For pharyngeal infections, variables accounted for in calculating adjusted prevalence ratios include Age and Sexual identity/Gender identity

PR stands for Prevalence Ratio

CI stands for 95% Confidence Interval