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Incident syphilis infection among people who inject drugs in Tijuana, Mexico

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Abstract

Given that syphilis is associated with HIV infection among people who inject drugs (PWID), we examined syphilis incidence among PWID in Tijuana, Mexico. From 2006–2007, 940 PWID (142 females and 798 males) were recruited via respondent driven sampling and followed for 18 months. At semi-annual visits, participants were tested for syphilis and completed surveys, which collected information on socio-demographics, sexual behaviors, substance use, and injection behaviors. Poisson regression was used to estimate syphilis incidence rates (IRs), incidence rate ratios (IRRs), and 95% confidence intervals (CIs). Twenty-one participants acquired syphilis during follow-up (IR=1.57 per 100 person-years, 95% CI: 1.02–2.41). In a multivariate analysis, syphilis incidence was higher among females (IRR=3.90, 95% CI: 1.37–11.09), HIV-positive participants (IRR=4.60, 95% CI: 1.58–13.39), and those who reported ever exchanging sex for drugs, money, or other goods (IRR=2.74, 95% CI: 0.97–7.76), while syphilis incidence was lower among those living in Tijuana for a longer duration (IRR=0.95 per year, 95% CI: 0.91–1.00) and those reporting daily injection drug use (past 6 months) (IRR=0.22, 95% CI: 0.09–0.54). Our findings suggest interventions that address the destabilizing conditions associated with migration and integrate sexual and drug-related risk reduction strategies may help reduce syphilis incidence among PWID along the Mexico-US border.

Keywords

syphilis; HIV; people who inject drugs; Mexico

Declaration of Conflicting Interests:

None declared.

Introduction

Although HIV acquisition among people who inject drugs (PWID) has historically been attributed to parenteral exposures resulting from risky injection practices,¹ sexual transmission accounts for a substantial proportion of HIV infections within this population.² Previous research conducted among PWID has also documented elevated rates of syphilis,³ which facilitates HIV transmission and enhances susceptibility to HIV during sexual intercourse.⁴ Interventions that promote testing for sexually transmitted infections (STIs), including syphilis, and address both sexual and drug-related risk behaviors are needed to reduce HIV transmission among PWID.

Tijuana, Mexico borders San Diego, California, and is positioned on a major drug trafficking route linking the United States (US) with South and Central America, which has contributed to an epidemic of injection drug use in the city.⁵ Although HIV prevalence remains under 5% among male PWID in Tijuana, the estimated prevalence among female PWID is higher at 10%.⁶ Similarly, a higher prevalence of active syphilis (titers 1:8) has been reported for female PWID (16%) than for male PWID (6%) in Tijuana, and active syphilis has also been independently associated with HIV infection within this population.⁶ Among female sex workers (FSWs) who inject drugs surveyed in the Mexico-US border region between 2004 and 2005, the estimated prevalence of active syphilis was 23%.⁷ In another study conducted among FSWs in the region, active syphilis was associated with injecting drugs, using illicit drugs before/during sex, and having clients from the US.⁸ Yet little is known about predictors of syphilis incidence among PWID in this region. To inform the development of syphilis control programs for PWID, we estimated the incidence and identified predictors of syphilis among PWID in Tijuana, Mexico.

Methods

Study design

From 2006–2007, 1056 PWID in Tijuana were recruited via respondent-driven sampling (RDS)⁹ to participate in a prospective (18 months) study of HIV, syphilis, and tuberculosis. As previously described,^{10, 11} diverse seeds (n=32) (heterogeneous with respect to age, gender, and geographic location) were selected and given uniquely coded coupons to refer their peers to the study. Eligible recruits were then given coupons to recruit their peers in subsequent recruitment waves. Men were given three coupons while women were given six to twelve coupons in an effort to recruit more women. Of the 32 seeds, 24 successfully recruited other PWID eligible for study participation. On average, there were 6.8 recruitment waves across the 460 recruitment chains (min=1; max=17). Eligible individuals were 18 years-old; reported injection drug use within the past month (verified by inspection of track marks); spoke Spanish or English; and had no imminent plans to move to another city. All participants provided informed consent and institutional review boards at the University of California, San Diego and Tijuana General Hospital approved all study protocols.

Study procedures

At semi-annual visits (four visits total), participants completed interviewer-administered questionnaires that collected information on socio-demographics, mobility, sexual behaviors, substance use, and injection behaviors. Participants provided blood samples for HIV and syphilis testing at each visit. Positive 'Determine' rapid HIV antibody tests (Abbott Pharmaceuticals, Boston, MA) were confirmed via Western blot. Syphilis infection was identified via rapid plasma reagin (RPR) testing (Macro-Vue; Becton Dickinson, Cockeysville, MD) of participants' sera and confirmed using the *Treponema pallidum* particle agglutination assay (TPPA; Fujirebio, Wilmington, DE). All specimen testing was conducted at the San Diego County Health Department. HIV or syphilis positive participants were referred to municipal clinics for free care and treatment.

Incident syphilis

Baseline RPR and TPPA results and RPR titers were considered in defining incident syphilis. Among participants without syphilis at baseline (i.e., RPR and TPPA negative or RPR and TPPA positive with RPR titers <1:8), incident syphilis cases were RPR and TPPA positive with RPR titers 1:8 at a follow-up visit. Among participants with syphilis at baseline (i.e., RPR and TPPA positive with RPR titers 1:8), incident syphilis cases self-reported treatment and had evidence of a 4-fold decrease in titers at a follow-up visit followed by a 4-fold increase in titers at a subsequent follow-up visit. Of the 1056 participants, 940 had data available at baseline and 1 follow-up visit to determine their incident syphilis status and were eligible for inclusion in our analysis.

Statistical analysis

For our analysis, participants were followed from enrollment to incident syphilis, loss to follow-up, or the end of the study period, whichever came first. Syphilis incidence was calculated by dividing the number of incident cases by the observed number of person-years. The date of syphilis infection was defined as the date of the visit at which the individual tested syphilis positive. Poisson regression was used to estimate syphilis incidence per 100 person-years. In an exploratory analysis, Poisson regression was used to identify predictors of incident syphilis. Predictors of interest included: socio-demographics, mobility, sexual behaviors, substance use, and injection behaviors. To minimize temporal ambiguity, we examined predictors measured at the second visit. Significant ($\alpha=0.05$) predictors in unadjusted analyses were examined for collinearity and considered for inclusion in our final adjusted model. If <5 incident syphilis cases were observed for a single level of a significant predictor (i.e., usual injection location), that predictor was excluded from our final model to minimize the potential for biased estimates due to small cell sizes. Because RDS-weighted and unweighted estimates were similar only unweighted results are presented.¹²

Results

Compared to participants with complete follow-up (858/1056), a greater proportion of participants with incomplete follow-up (198/1056) reported being deported from the US or tested positive for HIV at baseline. On average, those with incomplete follow-up also reported living in Tijuana for a shorter duration. Participants with data available at baseline

and 1 follow-up visit to determine their incident syphilis status (N=940) contributed 1,337.5 person-years (5% 0.5 person-years; 6% 1 person-years; 89% 1.5 person-years) to the analysis. Our sample (N=940) was mostly male (85%) and had a mean age of 37.3 years (SD=8.3) (Table 1). In the past 6 months, 97% of participants reported using heroin and 85% reported injecting drugs at least daily. Six percent (57/940) of participants tested positive for syphilis at baseline, and of those 47% (27/57) self-reported treatment at a subsequent visit.

Twenty-one incident syphilis infections (13 females and 8 males) were observed during follow-up (incidence rate=1.57 per 100 person-years, 95% CI: 1.02–2.41). Of participants with incident syphilis, 26% (5/19) self-reported treatment at a subsequent visit. In our final adjusted model (Table 2), syphilis incidence was higher among females (IRR=3.90, 95% CI: 1.37–11.09), HIV-positive participants (IRR=4.60, 95% CI: 1.58–13.39), and those who reported ever exchanging sex for money, drugs, or other goods (IRR=2.74, 95% CI: 0.97–7.76). Syphilis incidence was lower among those living in Tijuana for a longer duration (IRR=0.95 per year, 95% CI: 0.91–1.00) and those reporting at least daily injection drug use (past 6 months) (IRR=0.22, 95% CI: 0.09–0.54).

Discussion

In this cohort of PWID followed for 18 months in Tijuana, Mexico, the overall incidence of syphilis was 1.6 per 100 person-years – slightly lower than that observed in a cohort of PWID in Los Angeles County (2.6 per 100 person-years, 95% CI: 1.9–3.2).¹³ However, the rate of syphilis infection was nearly four times higher among females, which is consistent with reports from previous studies conducted among PWID reporting both a higher prevalence³ and incidence^{13, 14} of syphilis among females. Previous research has also documented an association between syphilis and trading sex or being paid for sex among PWID,^{13, 14} particularly female PWID,¹⁵ which may explain much of the observed association between gender and incident syphilis. In Mexico-US border cities, socially-marginalized women who inject drugs have limited employment opportunities and often engage in sex work to support themselves and their addictions.¹⁶ Although we were unable to stratify by gender, we observed an association between incident syphilis and ever exchanging sex for drugs, money, or other goods, which was reported by a greater proportion of females than males (62% vs. 18%). Thus, our findings underscore a need for gender-specific risk reduction strategies and suggest interventions designed to increase condom use with commercial sex partners may help reduce the risk of syphilis among female PWID.

Participants living in Tijuana for a longer duration were less likely to be diagnosed with syphilis during follow-up. This finding is consistent with the previously reported association between recent migration to Tijuana and HIV infection within our sample.^{6, 10} Migrant populations are highly prevalent in the Mexico-US border region as a result of both cross-border mobility between Mexico and the US and migration from within Mexico in search of economic opportunities in the region.¹⁷ Numerous studies have documented a relationship between migration and increased sexual risk behaviors and risky injection practices,^{18–20} which may be the result of changing social networks or an enhanced sense of anonymity in the new environment.²¹ However, migrants may also be driven to engage in high-risk

behaviors (e.g., substance use, sex work or sex with commercial sex workers) as a means of coping with the social and economic stressors (e.g., homelessness, difficulty securing employment, and family separation) associated with migration.²² Interventions targeting migrant PWID in the Mexico-US border region that minimize the destabilizing conditions associated with migration, and integrate strategies to reduce both sexual and drug-related risk behaviors may help control the spread of syphilis within this population.

Syphilis incidence was also lower among participants reporting daily injection drug use. In a study of male PWID in Vietnam, non-daily injection drug use was associated with chlamydial infection.²³ During in-depth interviews, these male PWID expressed decreased sexual interest or desire with increasing injection frequency.²³ Thus, decreased sexual activity may have similarly reduced syphilis exposure among PWID who reported daily injection drug use in our sample.

Although not statistically significant, syphilis incidence was higher among participants reporting elevated risk behaviors, such as having multiple casual sex partners, engaging in unprotected sexual intercourse, and practicing receptive needle sharing at least half the time in the past 6 months. Moreover, HIV-positive participants were also more likely to be diagnosed with syphilis during follow-up. While many HIV-positive individuals adopt lower risk behaviors following diagnosis,²⁴ others continue to practice high-risk behaviors,^{25, 26} which may have been the case within our sample and explain the observed relationship between HIV and incident syphilis. Given that nearly half of our sample reported obtaining syringes from the local needle exchange program (past 6 months), expanding such programs and incorporating risk reduction counseling, point-of-care STI/HIV testing, and on-site STI treatment may help reduce STI/HIV incidence among PWID in the Mexico-US border region.

Our study has several limitations. First, given the study's recruitment strategy, our findings may not be generalizable to all PWID in Tijuana. Second, although retention was high (81%), participants with complete follow-up differed from those with incomplete follow-up with respect to their baseline HIV status and duration of residence in Tijuana, which may have biased our estimate of incident syphilis downwards. Third, our definition of incident syphilis is limited to diagnosis as part of the study. Although unlikely, participants could have been diagnosed and treated for syphilis between study visits, which would have resulted in an underestimate of incidence. Fourth, data were collected via face-to-face interviews, thus participants may have under-reported sensitive information on substance use and sexual behaviors. However, study staff made every effort to build rapport with participants and earn their trust to minimize social desirability bias. Fifth, the low overall incidence of syphilis within our sample resulted in large confidence intervals and may have limited our power to detect predictors of incident syphilis. Finally, although enhanced efforts were employed to recruit female PWID, the small sample of women included in our study did not enable stratification by gender.

Despite these limitations, our findings underscore the need for syphilis control programs among PWID along the Mexico-US border. While additional research powered to investigate syphilis incidence among both male and female PWID is needed to inform the development

of effective interventions for this population, our findings suggest interventions that address the destabilizing conditions associated with migration and integrate sexual and drug-related risk reduction strategies may help reduce syphilis incidence among PWID in the Mexico-US border region.

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Table 1

Characteristics of PWID in Tijuana, Mexico.

	Female (N=142)	Male (N=798)	Total (N=940)
Characteristics [^]	n (%)	n (%)	n (%)
Socio-demographics			
Mean age in years (SD)	35.2 (8.6)	37.7 (8.2)	37.3 (8.3)
Mean years of education completed (SD)	7.9 (4.0)	7.2 (3.3)	7.3 (3.4)
Married/common law relationship	72 (50.7)	213 (26.7)	285 (30.3)
Average monthly income 3,000 pesos (~230 USD)	88 (63.3)	551 (70.6)	639 (69.5)
Ever arrested	120 (85.1)	727 (91.1)	847 (90.2)
HIV-infected	14 (9.9)	31 (3.9)	45 (4.8)
Syphilis at baseline	21 (15.1)	36 (4.5)	57 (6.1)
Mobility			
Mean years living in Tijuana (SD)	16.3 (14.1)	18.9 (15.1)	18.5 (15.0)
Ever traveled to the US	93 (65.5)	634 (79.5)	727 (77.3)
Ever deported from the US	30 (21.1)	351 (44.0)	381 (40.5)
Sexual behavior[~]			
Ever had sex with someone of the same gender	43 (30.5)	211 (26.4)	254 (27.1)
Ever exchanged for sex money/drugs/other goods	87 (61.7)	143 (17.9)	230 (24.5)
Ever been forced to have sex	40 (28.4)	6 (0.8)	46 (4.9)
>1 casual sex partner	42 (29.8)	87.0 (10.9)	129.0 (13.7)
Unprotected sex with regular/casual partners	76 (53.9)	195 (24.4)	271 (28.9)
Substance use[~]			
5 alcoholic drinks on one occasion (past month)	21 (14.9)	176 (22.2)	197 (21.1)
Heroin	135 (95.1)	772 (96.7)	907 (96.5)
Cocaine	12 (8.5)	85 (10.7)	97 (10.3)
Methamphetamine	102 (71.8)	510 (63.9)	612 (65.1)
Injection behavior[~]			
First injected drugs within the past 5 years	29 (20.6)	79 (10.0)	108 (11.6)
Injected drugs at least daily	122 (86.5)	664 (84.5)	786 (84.8)
Usually injected drugs alone	43 (30.3)	253 (31.7)	296 (31.5)
Usually injected drugs in a shooting gallery	32 (22.5)	377 (47.2)	409 (43.5)
Usually injected drugs outside	10 (7.0)	168 (21.1)	178 (18.9)
Receptive needle sharing half the time	23 (16.2)	143 (17.9)	166 (17.7)
Used local needle exchange program	69 (48.6)	326 (40.9)	395 (42.0)

Numbers may not sum to column totals due to missing values; Percentages may not sum to 100 due to rounding.

Abbreviations: PWID=people who inject drugs; SD=standard deviation; US=United States; USD=US dollar.

[^] Measured at visit 2 or visit 1 if no visit 2 data available.

^{*} Syphilis at baseline=rapid plasma reagin and *Treponema pallidum* particle agglutination assay positive with RPR titers 1:8.

[~] Past 6 months unless stated otherwise.

Table 2

Incidence rate ratios for syphilis among PWID in Tijuana, Mexico.

Characteristics [^]	Unadjusted		Adjusted	
	IRR	95% CI	IRR	95% CI
Socio-demographics				
Age (in years)	1.00	0.95, 1.05		
Female [*]	9.49	3.93, 22.93	3.90	1.37, 11.09
Years of education completed	1.01	0.89, 1.15		
Married/common law relationship	2.09	0.89, 4.93		
Average monthly income 3,000 pesos (~230 USD)	0.70	0.29, 1.70		
Ever arrested	1.05	0.24, 4.52		
HIV-positive [*]	7.15	2.62, 19.55	4.60	1.58, 13.39
Mobility				
Years living in Tijuana [*]	0.95	0.92, 0.99	0.95	0.91, 1.00
Ever traveled to the US	0.74	0.29, 1.90		
Ever deported from the US	0.46	0.17, 1.25		
Sexual behavior[~]				
Ever exchanged for sex money/drugs/other goods [*]	6.27	2.53, 15.56	2.74	0.97, 7.76
Ever been forced to have sex	3.31	0.97, 11.26		
>1 casual sex partner [*]	2.67	1.04, 6.89	1.13	0.41, 3.11
Unprotected sex with regular/casual partners [*]	2.79	1.18, 6.57	2.05	0.79, 5.34
Substance use[~]				
5 alcoholic drinks on one occasion (past month)	0.63	0.19, 2.15		
Heroin	0.33	0.08, 1.44		
Cocaine	1.41	0.42, 4.81		
Methamphetamine	0.86	0.36, 2.08		
Injection behavior[~]				
First injected drugs within the past 5 years	2.42	0.89, 6.62		
Injected drugs at least daily [*]	0.23	0.10, 0.55	0.22	0.09, 0.54
Usually injected drugs alone	1.34	0.56, 3.25		
Usually injected drugs in a shooting gallery [*]	0.005	0.002, 0.016		
Usually injected drugs outside [*]	0.008	0.002, 0.031		
Receptive needle sharing half the time	1.85	0.72, 4.78		
Used local needle exchange program	1.28	0.54, 3.02		

Abbreviations: PWID=people who inject drugs; IRR=incidence rate ratio; CI=confidence interval; US=United States; USD=US dollar.

[^] Measured at visit 2 or visit 1 if no visit 2 data available.[~] Past 6 month unless stated otherwise.^{*} Unadjusted IRR p-value 0.05.