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Short Report: Lack of Evidence of Hepatitis C and HIV Co-Infection among Men Who Have Sex with Men in Peru

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Abstract

Hepatitis C virus (HCV) infection occurs among human immunodeficiency virus (HIV)-infected men who have sex with men (MSM) because of shared routes of transmission. To assess the association between HCV and HIV infection among MSM in Peru, we conducted a matched case-control study (162 HIV-positive cases and 324 HIV-negative controls) among participants of an HIV sentinel surveillance survey in six urban cities. The HCV infection was initially screened using anti-HCV ELISA and immunoblot assay, and thereafter confirmed by the HCV RNA qualitative assay. Among cases, no confirmed HCV infection was found while among controls, only two confirmed HCV infections were reported (0.62%). This matched case-control reports a very low probability of association between HCV and HIV co-infection and suggests a very low prevalence of HCV infection among MSM in Peru.

Hepatitis C virus (HCV) infection occurs among human immunodeficiency virus (HIV)-infected men who have sex with men (MSM) because of shared routes of transmission.¹

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Human Use Statement: The study protocol (NMRC.D.2003.0003, DoD No. 32513, Second Generation Surveillance of STD/HIV/AIDS in Men Who Have Sex with Other Men (MSM), Peru-2002) was approved by the Asociacion Civil Impacta Salud y Educacion (Lima, Perú), and by the U.S. Naval Medical Research Center (Silver Spring, Maryland) Institutional Review Boards in compliance with all applicable federal regulations governing the protection of human subjects; and by the National AIDS and STD Control Program of the Ministry of Health of Peru.

The HCV infection is more common among people who have sexual contact with an HCV-infected partner; those who report multiple sexual partners; those of a younger age at first sexual encounter; and among MSM and heterosexual men who do not routinely use condoms.² In Latin America, high HIV prevalence (11–21%) among MSM communities has been reported.³ Although previous studies documented the epidemiology of HCV infection in multi-transfused patients, female sex workers, and blood donor populations; there is a lack of information on HCV infection among MSM in Peru. This is a population with high rates of HIV and sexually transmitted infections (STI), as well as high risk behavior.⁴ The purpose of this matched case-control study was to assess the association between HCV and HIV infection among MSM in Peru.

A second-generation HIV sentinel surveillance survey of 3,280 MSM was conducted in six urban cities (Sullana, Piura, Lima/Callao, Iquitos, Pucallpa, and Arequipa) in Peru during 2002–2003. Methodology on that study and its main results have been published elsewhere.⁴ In short, a convenience sample of men (at least 18 years of age) who reported sexual intercourse with men during the preceding year were invited to participate, regardless of history of HIV testing, serostatus, or treatment. Outreach work and “snowball” techniques were used to recruit participants. Recruiters and peer educators representing the diverse MSM sub-cultures in each city, visited different and previously mapped venues to contact potential participants and to refer them to sentinel sites, where one counselor explained the study objectives to participants and obtained written informed consents. Those participants who agreed underwent a computer-assisted self-interview, which included questions dealing with demographics, sexual risk behavior, previous HIV testing and diagnosis, self-designated sexual identity, self-reported past evidence of STI and illegal drug use in the recent past. All participants received pre- and post-test counseling, sexual risk behaviors reduction education, and condoms, as well as, sexually transmitted disease (STD) syndromic management when indicated.

To evaluate the objective of this study, a case was defined as a participant with an HIV-positive diagnosis and a control as a participant with an HIV-negative diagnosis. There were two controls matched to each case based on two criteria: age (± 1 year) and city; cases and controls were randomly selected.

The study protocol and informed consents were approved by the Asociacion Civil Impacta Salud y Educacion (Lima, Peru), by the U.S. Naval Medical Research Center (Silver Spring, MD) Institutional Review Boards, and by the National AIDS and STD Control Program of the Ministry of Health of Peru.

The HIV-1 serostatus was determined by enzyme-linked immunosorbent assay (ELISA) testing with the Vironostika HIV-1 Microelisa system (Organon Teknika, Durham, NC) with confirmation by the Genetic Systems HIV-1 Western blot (Bio-Rad Laboratories, Hercules, CA). Anti-HCV antibodies were screened using the ORTHO HCV 3.0 ELISA, (Ortho-Clinical Diagnostics, Raritan, NJ) and confirmed by the Chiron RIBA HCV 3.0 SIA immunoblot assay (Ortho-Clinical Diagnostics). A nucleic-acid amplification test for qualitative detection of HCV RNA was performed on all samples that tested positive or indeterminate by the Chiron RIBA using the AMPLICOR HCV test 2.0 (Roche Diagnostics Corporation, Indianapolis, IN). A confirmed case of HCV infection is one defined as a case found to be positive by HCV RNA.

We estimated that 162 cases (selected from among 456 participants diagnosed with HIV infection in the main study) and 324 controls (selected from 2,824 HIV-negative participants) would allow for detection of an odds ratio (OR) at least 2.0 or higher; given 80% power, a type I error of 0.05, and exposure prevalence ranging from 20% to 50%. The

χ^2 and Fisher's exact tests was used to compare proportions. Analyses were performed using STATA (version 8.0; Stata Corporation, College Station, TX).

The mean age of subjects was 27.4 years of age (median, 26 years; range, 18–58). Because of the matched design, cases and controls were comparable with respect to age and location (city) of enrollment. The case-control group was comparable to the larger sentinel surveillance survey population. Cases and controls were statistically different in terms of educational level, history of any STI, urethral discharge, genital ulcer, blood or pus from rectum, sex with HIV-positive partner, and self-identification as a homosexual (Table 1). There was no significant difference found in past evidence of illegal drug use. No study participants mentioned past injecting drug use (IDU) behavior.

There were initially 26 (16%) HCV ELISA reactive results found among cases. Of these samples, 3 were indeterminate and 23 were negative by immunoblot assay. The 3 indeterminate samples subjected to HCV NAT testing were found to be negative. Therefore, there were no confirmed HCV infections found among the cases. However, among controls, there were initially 20 (6.2%) HCV ELISA reactive results found. Of these, 2 samples were positive, 15 were negative, and 3 were indeterminate by immunoblot assay. By HCV RNA, 2 samples out of 5 (2 positive and 3 indeterminate by immunoblot) were confirmed to be HCV-positive (0.62%, 95% confidence interval [CI] = 0.08–2.21%).

Given the absence of confirmed cases of HCV infection among HIV-positive cases, and the very low rate among controls; no further statistical analysis was conducted to assess the association between HCV infection and HIV infection in conjunction with other covariables.

This study reports a lack of association between HCV and HIV co-infection and suggests a very low prevalence of HCV infection among MSM in Peru.

The association of HCV among HIV-infected MSM remains controversial, especially among MSM without a history of IDU. Differences in the study design and low sensitivity and specificity of early assays may explain these differences. A recent cohort MSM study reported an association of unsafe sex (inconsistent condom use) and incidence of HCV in HIV-infected MSM without an IDU history (hazard ratio = 3.0, 95% CI = 1.03–8.8).⁵ However, this association might be a surrogate for other non-sexual risk factors, such as acupuncture or tattooing and by sharing materials used for intranasal cocaine use. These factors were previously described as potential routes for acquisition of HCV infection,⁶ and we did not assess these non-sexual risk factors in our study. In addition, the duration of the relationship with the HIV-infected index case could also affect HCV transmission,⁷ something that was not evaluated by our group.

The overall HCV prevalence found in this study was similar in comparison with the baseline found in a recent cohort study of 1,054 MSM in Montreal, when the proportion of participants who were IDU was excluded (0.31%, 95% CI = 0.06–0.89).⁵ In our study population, low rates of illegal drug use (approximately 20%) were observed, and total absence of previous IDU behavior. This may explain the low probability of HCV transmission among MSM in Peru, where it has been associated with unsafe injection-related and medical/dental procedures and HCV genotype 1 accounts in the majority of the studied cases.⁸

The high number of participants with anti-HCV without HCV RNA may suggest that these individuals have recovered from a previous HCV infection and might go on to be at risk for liver disease later in life.⁹ Alternatively, it is possible that we have seen a high rate of false-positives with anti-HCV testing. This is something that can be quite common (in as many as 15–60% of cases), especially among immunocompetent populations with anti-HCV

prevalence less than 10%, suggesting a very low positive predictive value of the ELISA methodology in low prevalence settings. The role other members of the flaviviridae family prevalent in Peru (e.g., yellow fever, dengue fever) may have in inducing false positive HCV ELISA results needs to be further evaluated. According to the U.S. Centers for Disease Control and Prevention (CDC) guidelines,¹⁰ after an anti-HCV screening-test-positive result, this should be confirmed by a more specific serologic test (immunoblot assay) or a nucleic acid test. In addition, a recently published study strongly suggests that HCV RNA is mainly detected in persons with high signal-to-cutoff ratio greater than 3.8.¹¹ Interestingly the two HCV-positive persons detected by immunoblot assay and HCV RNA in our study had an average signal-to-cutoff ratio greater than 3.9.

In summary, this is the first study evaluating the association between HCV and HIV among MSM in Peru or any other Andean region countries. In Peru, the HIV prevalence in the MSM population was estimated to approximately range between 5.7% and 22.3% in major urban and populated cities.⁴ Our study findings indicate no association of HCV with HIV infection among MSM in Peru. Although our study could not directly assess the risk of sexual transmission of HCV among MSM given the overall rarity of HCV infection, it supports a growing body of evidence¹² that MSM who do not engage in IDU, have a low risk of HCV infection. Further studies of the potential association between HIV and HCV (and other blood-borne or sexually transmitted viral pathogens) should be able to better assess these relationships.

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Table 1

Characteristics of matched cases and controls among MSM in Peru

Feature	Cases (N = 162) n (%)	Controls (N = 324) n (%)	P value*
Low educational level (primary or less)	23 (14.2)	26 (8.0)	0.049
History of any STI	49 (30.4)	64 (19.8)	0.009
Urethral discharge in the past year	16 (9.9)	15 (4.6)	0.025
Genital ulcer in the past year	25 (15.5)	30 (9.3)	0.042
Blood or pus from rectum	26 (16.2)	26 (8.1)	0.007
Genital warts in the past year	14 (8.7)	21 (6.5)	0.380
Four or more sexual partners in the 3 mo	41 (25.3)	90 (27.8)	0.563
Sex with HIV-positive partner	65 (79.3)	115 (66.9)	0.042
Homosexual definition	121 (74.7)	206 (63.8)	0.016
Sex without condom	11 (13.4)	15 (8.7)	0.249
Work as a sex worker	33 (55.9)	53 (51.0)	0.541
Oral insertive sex with last partner	60 (48.8)	130 (56.0)	0.192
Oral receptive sex with last partner	24 (19.5)	48 (20.7)	0.793
Anal receptive sex with last partner	43 (35.0)	77 (33.2)	0.737
Anal insertive sex with last partner	20 (16.3)	52 (22.4)	0.170
No consistent use of condoms	30 (34.1)	54 (31.6)	0.683
No use of condom in sex work	23 (69.7)	32 (60.4)	0.381
Any illegal drug use in the past 3 months	32 (19.8)	61 (18.8)	0.807
Marihuana use in the past 3 months	11 (7.8)	33 (11.1)	0.277
Cocaine use in the past 3 months	25 (16.1)	43 (14.1)	0.552
Illegal drug use before/during sex	17 (10.5)	29 (9.0)	0.701
Alcohol use before/during sex	84 (67.2)	195 (72.8)	0.098

MSM = men who have sex with men; STI = sexually transmitted infection; cases = human immunodeficiency virus (HIV)-positive subjects; controls = HIV-negative subjects.

*P-value by χ^2 or Fisher's exact test.