

Hepatitis and Human Immunodeficiency Virus Co-Infection Among Injection Drug Users in Los Angeles County, California

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ABSTRACT. This study examined the prevalence of hepatitis A (HAV), B (HBV), C (HCV), and Human Immunodeficiency Virus (HIV) co-infection among Injection Drug Users (IDUs) in Los Angeles County, California, and predictors of multiple infections in this population. Six hundred seventy-nine IDUs were recruited from October 2002 through June 2004. Participants completed questionnaires to elicit demographic, drug and sex risk information, and were tested for hepatitis A, B, C and HIV. A linear regression model predicting the total number of infections (0 to 4 possible) was constructed. Significant associations were found between HAV and HBV infection, HAV and HCV infection, and HBV and HCV infection. Predictors of total co-infections included age of first injection, lifetime years in jail, and Hispanic ethnicity. Latinos had the highest proportion of HAV and HBV co-infection with HCV. The total number of co-infections, especially those co-infected with all three of the hepatitis infections, was unexpectedly high. [Article copies available for a fee from The Haworth Document Delivery Service: 1-800-HAWORTH. E-mail address: <docdelivery@haworthpress.com> Website: <<http://www.HaworthPress.com>> © 2006 by The Haworth Press, Inc. All rights reserved.]

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INTRODUCTION

Injection drug users are at high risk for several infectious diseases, including HIV, and hepatitis A, B, and C. Hepatitis A (HAV) has been associated with Hispanic populations re-

siding along the U.S.-Mexico border,¹ Latino homosexual and bisexual men² and with injection drug users (IDUs).^{3,4} The disease rate for Latinos in Los Angeles County has been reported to be many times higher than Anglos or Blacks.⁵ The mode of transmission is usually

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person-to-person through the oral-fecal route, although exposure through water and food-borne transmission also occurs.¹ Outbreaks of HAV in IDUs have been reported in the United States,^{6,7} Australia,⁸ Finland,⁹ and Canada.¹⁰

Hepatitis B (HBV) exposure can occur through sexual, blood-borne, or household transmission. Individuals contracting HBV may either recover from the infection, or become carriers of the disease. Individuals screened at sexually transmitted disease clinics have shown high rates of HBV, especially among those reporting any injection drug use or men reporting sex with men.^{11,12} A study of homeless veterans in Los Angeles County revealed that HBV infection in this population was high compared to the general U.S. population.¹³ This study also found injection drug use to be highly associated with HBV infection.¹³ Another study in Los Angeles also found high rates of HBV infection in individuals who were recently released from detention,¹⁴ with injection drug use while in detention being one of the primary risk factors for infection. Among drug injectors in the United States, minorities such as Hispanics and African Americans are disproportionately infected with hepatitis B and C.¹⁵

Drug users are at elevated hepatitis C risk through shared injection equipment.¹⁶⁻¹⁹ Hepatitis C is currently the most common chronic blood-borne infection in the United States²⁰ with the Centers for Disease Control and Prevention estimating that nearly 4 million Americans are HCV infected, and the California Department of Health Services estimating that a total of 600,000 Californians are infected with hepatitis C.²¹ The majority of individuals testing positive for HCV were exposed through injection drug use. Up to 20 percent of those with the virus go on to develop advanced liver disease such as scarring or cirrhosis. One to five percent of infected people progress to liver cancer. Differences in genetic make up between racial ethnic groups appear to influence viral clearance of hepatitis C. Thio et al.²² reported that HCV clearance occurs less often in African Americans and in Human Immunodeficiency Virus (HIV)-infected persons. In two recent studies of HCV-infected racial/ethnic minorities in Los Angeles County,^{23,24} Latinos were found to show significant differences in ALT, aspartate transaminase, bilirubin, and albumin

levels compared to other groups²³ and to progress to liver fibrosis faster than Whites or African Americans.²⁴

HCV prevalence is approximately three times higher for individuals between the ages of 30 and 49 years old than for those in either older or younger age groups.²⁰ Up to 90% of injection drug users are infected with HCV.²⁵ Among injection drug users, sharing of non-sterile injection equipment and greater numbers of years injecting are both strong predictors of HCV positivity.²⁶ Substantial risk of HCV infection has also been linked to sharing injection paraphernalia including cookers, cotton and water.²⁷

High rates of HCV infection have been found in California in a number of samples, including inmates in the correctional system, with the highest prevalence found in White men and Latina women;²⁸ in veterans who also reported previous injection drug use;²⁹ in patients in methadone maintenance treatment;³⁰ in homeless adults, especially those with lifetime histories of injection drug use;³¹ in HIV-infected homeless individuals who report injection drug use and severe depression;³² and in racial/ethnic minority groups.^{23,24}

A recent review of the literature on HIV and HCV infection among injecting drug users³³ indicates that, worldwide, in injection drug users, HIV prevalence varies from < 5% to > 80%, with annual HIV incidence between 1% to 50%. These researchers found more consistency in reported rates of HCV infection among injection drug users than they found in reports of HIV incidence or prevalence. HCV prevalence ranges from 50-90%, and annual incidence is reported to be between 10%-30%. These findings indicate that HIV transmission efficiency is lower than HCV transmission efficiency. Thio et al.³⁴ evaluated 559 HIV positive individuals and found that 97.8% were also HCV infected.

The purpose of this paper is to report on a study of injection drug users in Los Angeles County to assess the prevalence of hepatitis A, B, and C, and HIV, and then to determine predictors of having multiple infections (i.e., hepatitis and HIV co-infection) among this population.

METHOD

Participants

A total of 679 current or former injection drug users were recruited from drug treatment programs, methadone maintenance programs, needle exchange programs and from a community-based agency during the period October 2002 through June 2004. These sites were all located in the western part of Los Angeles County, ranging from Long Beach in the south to Venice in the north. The largest number of participants was recruited from residential drug treatment programs (41%), followed by 34 percent recruited from a community-based program offering HIV prevention programs, 19 percent recruited from methadone maintenance treatment programs (MMT), 5 percent recruited from needle exchange programs (NEP), and the remainder, which comprised less than 1 percent of clients, were recruited from an outpatient treatment program that was not an MMT. Eligibility for inclusion in the study required that participants be at least 18 years of age and have visible sign of injection ("track marks") based on the classification system developed by Cagle et al.³⁵ The age of participants ranged from 18 to 71 years ($M=42.9$ y, $SD=9.6$), 484 (66.5%) were male, and the racial/ethnic breakdown included 360 White, non-Hispanics (49.5%), 182 Hispanics (25%), 149 African Americans (20.5%), 12 Native Americans (1.65%), 6 Asian Pacific Islanders (< 1%), and 19 individuals who reported their race/ethnicity as Other (2.6%).

Questionnaires

As part of their involvement in this project, participants completed a variety of instruments designed to elicit information on drug use risk, injection practices, sexual risks, and other risk factors related to both hepatitis and HIV. These questionnaires included the Risk Behavior Assessment (RBA);³⁶⁻³⁹ and the Designer Drug Trailer (DDT), developed for use in conjunction with the RBA to elicit information on the use of so called "designer drugs" such as ecstasy (MDMA), Ketamine, and GHB.

Hepatitis Serostatus

All participants received pre-test counseling for hepatitis A, B, C, and HIV; all pre-test protocols for hepatitis followed the guidelines promulgated by the Centers for Disease Control and Prevention (CDC) and all pre-test protocols for HIV testing followed guidelines determined by the County of Los Angeles, Office of AIDS Programs and Policy (OAPP) and the State of California Office of AIDS. Blood was then drawn by a certified phlebotomist, and tested for hepatitis A, B, and C seromarkers. The test for hepatitis A was the HAVAB[®]EIA enzyme immunoassay for the qualitative detection of total antibody to hepatitis A virus (anti-HAV), and the test for hepatitis B was the hepatitis B virus core antigen (Recombinant) corzyme[®] enzyme immunoassay for the qualitative determination of total antibody to hepatitis B virus core antigen. Two tests were used for hepatitis C, depending upon the condition of the participants' veins. If participants were able to undergo phlebotomy and a blood sample could be obtained in this manner, the hepatitis C virus encoded antigen (Recombinant c100-3, HC-31, and HC-34) Abbott HCV EIA 2.0 enzyme immunoassay for the qualitative detection of antibody to hepatitis C virus (anti-HCV) was used. For participants for whom phlebotomy was not an option due to vein damage (68 participants fell into this category), the Home Access Health Corporation's test was used. This test requires only a drop of blood from a finger stick. The participants underwent the same pre-test counseling for hepatitis C as the other participants, however, due to the inability to obtain a large blood sample, they did not undergo testing for hepatitis A and B. Test results were provided in the same format for the home test kits as for the results obtained through venipuncture, that is, participants returned to the testing site and a counselor provided test results and a post-test counseling session explaining the results. The Orasure[®] HIV-1 oral specimen collection device swab test for HIV was used for participants who were tested for hepatitis C using the Home Access Health Corporation test kit.

Procedure

All participants were screened for visible signs of injection before being admitted to the study using procedure developed by Cagle et al.³⁵ After eligibility was determined, informed consent was obtained, using a form approved by the California State University, Long Beach, Institutional Review Board. After informed consent, all questionnaires were administered, followed by pre-test counseling and phlebotomy (or if phlebotomy was not possible, a finger stick). Lastly, participants were paid \$10 for their time and were provided with the date on which they could receive their test results. For testing completed using phlebotomy, this was one week after the blood draw. For the finger stick, the test result was not available until three weeks later. All participants testing positive for any infection were provided with referrals for additional medical follow-up, including liver function testing for those who were hepatitis C positive, and for medical care and case management services, for those testing positive for HIV.

RESULTS

Multiple Infections

Of the 679 participants, 609 were tested for hepatitis A and of these, 297 (48.8%) tested positive; 609 were tested for hepatitis B, and of these, 320 (52.5%) were positive; 679 were tested for hepatitis C (both types of tests combined) and of these 473 (69.7%) were positive, and 588 were tested for HIV, with 23 (3.91%) testing positive for HIV. The mean number of infections for the entire sample was $M = 1.64$ ($SD = 1.14$).

Test results were coded as either 0 = negative, or 1 = positive and all test results for each participant were summed. To determine the co-infection of participants among the four viruses, a 0-4 summation was created to account for the possible combinations of positive test results (0 positive results, 1 positive result, 2 positive results, 3 positive results, or all 4 positive results). These results can be seen in Table 1.

TABLE 1. Frequency of Multiple Infections in IDUs ($N = 683$)

Total Infections	Frequency %
0	137 (20)
1	198 (29)
2	134 (20)
3	209 (30)
4	5 (< 1)

The most common configuration was for individuals who tested positive for three infections ($n = 209$). Of these, 205 tested positive for all three hepatitis infections. Of those individuals testing positive for two infections ($n = 134$), the breakdown was as follows: 11/134 (8%) tested positive for the combination of hepatitis A and hepatitis B, 44/134 (33%) tested positive for hepatitis A and hepatitis C, and the most frequent combination among those testing positive for two infections was 79/134 (59%) who tested positive for both hepatitis B and hepatitis C. Several significant associations were found with respect to co-infections. Infection with HAV was significantly associated with co-infection with HBV ($\chi^2_1 = 77.14, P = 0.0001$). Infection with HAV was also highly associated with co-infection with HCV ($\chi^2_1 = 58.52, P = 0.0001$). Infection with HBV was highly associated with HCV co-infection ($\chi^2_1 = 137.59, P = 0.0001$).

Table 2 shows that there was a significant overall association between race/ethnicity and testing positive for each of the hepatitis infections [HAV ($\chi^2_5 = 27.83, P = 0.0001$), HBV ($\chi^2_5 = 16.23, P = 0.0062$), and HCV ($\chi^2_5 = 19.03, P = 0.0019$)] with Hispanic/Latino participants being more likely to test positive for any of the hepatitis infections than members other racial/ethnic groups.

Table 3 shows the hepatitis co-morbidity results. The chi-square tests of homogeneity are significant for all three two-way co-morbidity combinations. Even though Native Americans had the highest proportion of HCV with HBV co-morbidity, the Hispanics made the greatest contribution to the overall chi-square, and in all three combinations, the Hispanic group had significantly more co-morbidity than expected. For the gender ratio (% male) by ethnicity anal-

TABLE 2. Race by Hepatitis Comorbidity

Race	HCV & HBV*	HAV & HBV†	HAV & HCV‡	HCV & HIV§
Asian	2/6 = 33%	2/6 = 33%	3/6 = 50%	0/3 = 0%
Black	52/118 = 44%	36/118 = 31%	41/118 = 35%	3/85 = 4%
Hispanic	93/155 = 60%	81/155 = 52%	94/155 = 61%	6/129 = 5%
Native	7/11 = 64%	5/11 = 45%	6/11 = 55%	1/7 = 14%
Other	9/18 = 50%	6/18 = 33%	7/18 = 39%	0/11 = 0%
White	121/307 = 39%	79/307 = 26%	100/307 = 33%	7/214 = 3%

* $\chi^2_5 = 19.6$, $P = 0.0015$. † $\chi^2_5 = 33.7$, $P = 0.0001$. ‡ $\chi^2_5 = 36.7$, $P = 0.0001$. § $\chi^2_5 = NS$.

TABLE 3. Multiple Regression Predicting Total Number of Co-Infections Among IDUs

Variable	B	Standard Error B	β
Intercept	-0.179	0.211	0
Age at Interview	0.043	0.004	0.369
Lifetime years in jail	0.022	0.006	0.138
Ever used heroin-cocaine mixed	0.417	0.084	0.179
Highest grade of school completed	-0.053	0.021	-0.091
Age first time injected drugs	-0.017	0.005	-0.127
Latino/Ethnicity	0.295	0.094	0.112

R-square = 0.3229. Adjusted R-square = 0.3157.

ysis for those who are HCV positive only, we report the following: Black 67/92 = 73%, White 171/245 = 70%, Hispanic 96/147 = 65%, Asian 3/3 = 100%, Native 4/11 = 37%, Other 6/13 = 46%. This was significant $\chi^2_5 = 11.1$, $P = 0.0486$. In this case the Native American group had the largest contribution to the overall chi-square. We analyzed age by ethnicity and found that Blacks were the oldest at 46.6 y (SD = 8.9), followed by Natives at 44.7 y (SD = 8.3), Hispanics at 43.5 y (SD = 9.4), Whites at 41.8 y (SD = 9.6), Asians at 41.1 y (SD = 8.8), and Other at 40.3 y (SD = 9.5) $F_{5,717} = 5.78$; $P = 0.0001$. Further analysis with Tukey's pairwise comparison procedure finds that the Black-Hispanic and the Black-White differences are significant. Given that all of our participants are either former or current injection drug users, we could not assess whether the presence or absence of this risk factor was different by ethnicity, but we could assess the amount of injection drug use. For the number of times injected drugs in the 30 days prior to interview, we obtain a significant overall model $F_{5,717} = 2.56$, $P = 0.0261$. Asians were the highest at a mean of 31, followed by Other at 20, Hispanic at 18, White

at 12, Black at 8, and Native at 5. A Tukey procedure finds that the Hispanic-Black difference is significant.

Multiple Linear Regression Analysis

A linear regression predicting the number of total infections was determined, using variables from the Risk Behavior Assessment as independent variables. SAS version 9.1 for windows 2000 was used for all analyses.⁴⁰ The results of the test for collinearity indicate that all of the Variance Inflation Factors for the independent variables were below 1.5 and that only one condition index was above 10 at 15.4. No principal component had more than one variable with a proportion of variation greater than .5. The final, parsimonious regression model predicting number of co-infections can be seen in Table 3. This model accounts for 32 percent of the variation in the dependent variable, total number of infections.

DISCUSSION

This study reported on the prevalence of hepatitis A, B, and C and HIV in a sample of injection drug users recruited in Los Angeles County. As expected we found that rates among IDUs for hepatitis C were quite high, but within the bounds to be expected based on reports of prevalence among IDUs elsewhere in the United States. This study also found high rates of co-infection with hepatitis A and B, in addition to infection with hepatitis C, and this was surprising. The burden of hepatitis in this population is high, with just over 30 percent of the sample testing positive for all three hepatitis infections.

This high burden of hepatitis has public health implications. One of the public health responses to high rates of hepatitis C in IDUs is the recommendation that they be vaccinated against hepatitis A and B.^{18,41} However, in some populations such as this one, where antibodies already exist to hepatitis A and B, recommendations have been that testing first, before vaccination, may be the preferred approach due to its cost effectiveness.^{42,43} In this way, scarce public health funding for adult vaccinations can be maximized, and those IDUs who do

not have antibodies for hepatitis A and hepatitis B can be targeted for vaccination. The limitation to this approach is that without the additional testing for HAV and HBV antibodies, which currently must be done through phlebotomy, it is not possible to know what the infection rates are. For those IDUs for whom phlebotomy is not an option due to disintegrating veins, vaccination without testing may be the only viable alternative. It is our recommendation that when health care providers in Los Angeles County order laboratory tests for hepatitis C, they also order reflex tests for hepatitis A and B as a matter of routine.

The major findings from the regression model are that the older the participants were when we interviewed them, the more time they spent in jail, whether they had ever injected speedball (combination of heroin and cocaine), whether they were Latino, and the younger the age at which the IDUs first started injecting drugs, the greater the number of infections. The more education they had, the lower the number of infections. Even with all the other variables in the model, Latinos still had more infections than other ethnicities.

Both having spent time in jail and increasing age have been previously reported in the literature as being associated with HCV infection.^{31,44-46} The use of speedball, has also been reported in other studies as being a factor associated with risky injection practices and HIV infection.⁴⁷ Education has been found to be associated with a lower probability of needle sharing, which may explain its inclusion in our model.⁴⁸ There were very strong associations found between testing positive for each of the three hepatitis infections (HAV, HBV, and HCV) and Hispanic/Latino race/ethnicity, with more Hispanics/Latinos than expected by chance testing positive for each infection; this group was also more likely to test positive for three infections. It is possible that injection drug use risk factors also interact with other risk factors for these participants, such as travel to Mexico or the U.S.-Mexico border region and food-borne exposure to HAV as described by Weinburg et al. (2004) to place this group at high risk for multiple hepatitis infections.¹

There are some limitations to be noted about this study. First, our funding was limited so additional testing for hepatitis A and B positive in-

dividuals could not be conducted. We were focused on obtaining prevalence rates for this part of Los Angeles County, and did not have the funding to determine whether individuals testing positive for hepatitis B were carriers. The same was true for hepatitis A, in that we did not test for IgM and were not able to identify those participants falling in the 6-week period during which they would be infectious to other people for hepatitis A. We also did not have funding to conduct HCV PCR testing to determine genotype and viral load that can be done quite reliably.⁴⁹

Even though our sample is composed entirely of either former or current injection drug users, we sampled from a large proportion of Los Angeles County and have a fairly large sample. Given that all of our participants had injected drugs at some point in their lives, we tested whether there was any difference in the number of injections in the 30 days prior to interview. This is a commonly analyzed variable in the Risk Behavior Assessment which is a structured questionnaire commonly used in drug abuse research. We found that Asians had the most injections, and Whites and Hispanics were somewhat in the middle. We found HCV-HBV co-infection to be highest in Natives and Latinos and lowest in Asians. We found that men comprised the majority of our sample, however we found high proportions of female IDUs in Natives and Others. This finding of a high proportion of female IDUs is consistent with other data on American Indian and Alaska Natives.⁵⁰⁻⁵³

This paper reported on the high prevalence rates of hepatitis in current and former drug injectors in Los Angeles County, especially Hispanic IDUs. There is an urgent need for Spanish-language educational materials for this population, at a Spanish reading level that they can understand. Harm reduction, vaccination, and education efforts need to continue with IDUs to reduce overall prevalence in this population.

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