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Implications of hepatitis C viremia vs. antibody alone on transmission among male injecting drug users in three Afghan cities☆

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SUMMARY

Objectives: To assess differences between injecting drug users (IDUs) with hepatitis C virus (HCV) viremia and IDUs with HCV antibody (Ab) or no evidence of prior infection in three Afghan cities.
Methods: IDUs in Hirat, Jalalabad, and Mazar-i-Sharif completed questionnaires and rapid testing for blood-borne infections including HCV Ab. HCV Ab was confirmed with a recombinant immunoblot assay (RIBA); RIBA-positive specimens underwent reverse transcriptase polymerase chain reaction (RT-PCR) for HCV. Risk behaviors associated with viremia were assessed with site-controlled ordinal regression analysis.
Results: Of 609 participants, 223 (36.6%) had confirmed HCV Ab. Of 221 with serum available for PCR evaluation, 127 (57.5%) were viremic. HCV viremia prevalence did not differ by site (range 41.7–59.1%; $p = 0.52$). Among all IDUs, in age and site-controlled ordinal regression analysis, HCV was independently associated with HIV co-infection (adjusted odds ratio (AOR) 7.16, 95% confidence interval (CI) 4.41–11.64), prior addiction treatment (AOR 1.95, 95% CI 1.57–2.42), ever aspirating and re-injecting blood (AOR 1.62, 95% CI 1.18–2.23), prior incarceration (AOR 1.60, 95% CI 1.04–2.45), and sharing injecting equipment in the last 6 months (AOR 1.35, 95% CI 1.02–1.80).
Conclusion: HCV viremia was present in many participants with prior HCV infection and was associated with some injecting risk behaviors, indicating a substantial risk for transmission. Current harm reduction programs should aim to improve HCV awareness and prevention among IDUs in Afghanistan as a matter of urgency.

1. Introduction

Hepatitis C virus (HCV) is a serious health threat for injecting drug users (IDUs), among whom risky practices such as sharing syringes, other injecting equipment, or drug preparations may transmit infection.[1] HCV-associated morbidity among IDUs may manifest as hepatic failure and cirrhosis from chronic infection; this process may be accelerated and amplified by co-infection with HIV or hepatitis B virus (HBV).[1] Acute HCV is symptomatic in 10–15% of cases; those who are asymptomatic in the acute phase of infection are more likely (85–95% vs. 48–75%) to progress to chronic infection.[2]

Injecting drug use is a primary mode of transmission for HCV in developed countries. In developing countries, HCV transmission more commonly results from transfusion and unsafe medical practices.[1,2] However, HCV among IDUs in developing countries has been acknowledged as a burgeoning health issue, particularly in settings where HCV transmission is considered a harbinger of HIV epidemics among this population.[3–5] High HCV prevalence has been recorded among IDUs in many Asian settings, including Pakistan, India, and Iran, several of which are also high HCV burden countries (general population prevalence >2.9%).[1,6–9] The HCV prevalence found among IDUs in two urban settings in Afghanistan has been shown to range from 36.6% to 49.1% and may increase due to the risk of both injection-related and other potential exposures.[10,11] Increasing numbers of IDUs in Afghanistan and the common practice of sharing needles, syringes, injecting equipment

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and aspirating and re-injecting one's blood ('khoon bozee', literally 'playing with blood') may also contribute to an increasing prevalence of HCV among Afghan IDUs.[10,12]

Longitudinal studies have indicated that some IDUs previously infected with HCV are able to clear subsequent infections; this association persisted after adjustment for risky behaviors.[13,14] However, the risky behaviors that increase the likelihood of re-infection also increase the likelihood of HCV transmission to other IDUs due to the presence of viremia in re-infected individuals. IDUs with measurable viremia may differ significantly with respect to risky behaviors from those with either evidence of past infection or no evidence of prior infection, and are of special interest due to their ability to transmit infection to others. IDUs with viremia may also differ by biological factors; however, it is important to assess the relative association of behavioral factors, as these may be addressed through prevention programs. Our previous cross-sectional study in Kabul was conducted prior to the availability of nucleic acid testing in Afghanistan, so no information could be obtained regarding prevalence and traits associated with viremia. The data presented in this manuscript result from the follow-on assessment conducted between 2006 and 2008 in three other Afghan urban centers.

Recent data from a longitudinal study among IDUs in Kabul revealed high HCV incidence in a setting with many new injectors.[15] Assessment of whether IDUs with detectable viremia are distinct from those with antibody alone may provide important information to prevention programs in other Afghan cities to avert the HCV epidemic currently underway in Kabul. The purpose of this analysis was to determine whether the sub-group of IDUs with HCV viremia differs significantly from IDUs with either no evidence of prior infection or HCV antibody (HCV Ab), and to determine whether behaviors associated with HCV infection are more likely among IDUs with HCV viremia in three Afghan cities.

2. Methods

2.1. Setting

This study was conducted among IDUs in Hirat, Mazar-i-Sharif, and Jalalabad, the largest cities in their respective regions of Afghanistan. At the time of this study, private and public detoxification programs were operating in all cities; there was one harm reduction program operating in the city of Hirat with on-site needle exchange. The other two cities did not have functioning needle and syringe programs (NSPs) and no city had programs offering either opioid substitution therapy or the hepatitis B vaccine to IDUs at the time of the study.

2.2. Study design and participants

This cross-sectional study enrolled participants between September 2006 and January 2008 through the Ministry of Public Health-affiliated Voluntary Counseling and Testing centers (VCT), public and private harm reduction outreach programs (a few of which had VCT services on offer within their organizations), and the International Rescue Committee (IRC) offices in each location. Eligible participants were those reporting injecting drugs (confirmed through physical evidence of recent injection) within the past 6 months, aged 18 years or older, and who were able to provide written informed consent. Participants answered a series of questions to ensure comprehension of the study risks and benefits and the requirements of participation; participants unable to sign their name provided a fingerprint. Approval was obtained from the institutional review boards of the University of California, San Diego, the Walter Reed Army Institute of Research, the US Naval Medical Research Unit 3 in Cairo, Egypt, and the Ministry of Public Health of the Islamic Republic of Afghanistan.

2.3. Measurement of variables and outcomes of interest

The outcomes of interest for this analysis were the determination of whether IDUs with HCV viremia differ significantly from those with prior HCV infection and whether the association between HCV infection and various risky behaviors strengthens in a continuum from seronegative to viremic status. The questionnaire instrument assessed sociodemographic factors, travel, incarceration and medical histories, and drug use and sexual behaviors. Drug use behaviors of interest included sharing needles/syringes ever and in the last 6 months, sharing injecting 'works' (e.g., cookers, cotton) ever and in the last 6 months, duration of injecting, injecting while incarcerated, and aspirating and re-injecting blood. Iatrogenic routes of blood-borne infection transmission were also assessed, such as the receipt of therapeutic injections from both medical and non-medical providers and both the provision and receipt of transfused blood.

2.4. Procedures

Potential participants were recruited by experienced outreach workers affiliated with local harm reduction programs in each city. Trained study staff obtained informed consent, administered the study questionnaire, and performed rapid testing and counseling in a private setting. Laboratory methods for other pathogens have been reported in a related publication.[16] Briefly, whole blood rapid testing for HCV Ab was performed using Standard Diagnostics HCV Ab (Standard Diagnostics, Kyonggi-do, Korea). The manufacturer reports 100% sensitivity and 94.1% specificity by World Health Organization (WHO) evaluation.[17] Serum specimens were obtained from participants with positive rapid tests; HCV Ab was confirmed with a recombinant immunoblot assay (RIBA 3.0 SIA®, Chiron Corp., Emeryville, CA, USA). The presence of HCV was assessed with a qualitative reverse transcriptase polymerase chain reaction (RT-PCR). Extraction was performed using the QiAamp Viral RNA Mini Kit (Qiagen Inc., Germantown, MD, USA) according to the manufacturer's instructions. A nested RT-PCR was performed as previously described, with minor modifications of cycle parameters and master mix components.[18] Both RIBA and PCR were performed at the Afghan Public Health Institute laboratory in Kabul, with the exception of HBV PCR, which was performed at the United States Naval Medical Research Unit 3 (NAMRU-3) laboratory in Cairo, Egypt.

Confirmatory results were available after 2 weeks; participants were provided with follow-up appointments at the time of enrollment. All participants received post-test counseling, risk reduction counseling, a small non-monetary gift of hygiene items (e.g., razor, soap) of US$4 value, condoms, and sterile syringes, with referrals for detoxification programs upon request. No data were recorded on those declining or ineligible for study entry. Enrollment was conducted for 12 months at all sites.

2.5. Statistical analysis

Descriptive statistics for viremic individuals were generated, with site differences assessed using the Chi-square test. Risky behaviors, such as sharing syringes and injecting works, were reported by frequency; these variables were dichotomized into ever/never in the last 6 months.

Univariate logistic regression was performed to identify potential associations between HCV viremia and select demographic, biological, and individual risk behavior variables, controlled by enrollment site, of all confirmed HCV Ab-positive participants. Variables were entered into a site- and age-adjusted multivariable model if they were associated with HCV viremia at