Hepatitis C in Puerto Rico: a time for public health action

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Studies investigating the seroprevalence of HCV infection have been carried out in diverse populations, showing an estimated worldwide prevalence of 3%. A seroprevalence survey conducted among randomly selected non-institutionalized adults aged 21-64 years in San Juan, Puerto Rico in 2001-2002 revealed that 6.3% were positive for HCV antibodies. These data suggest that Puerto Ricans are burdened with a significantly greater prevalence of HCV infection compared to the general United States population aged 20-69 years (0.9%-4.3%). This article illustrates data from different sources that taken together establish the need to start addressing HCV infection in Puerto Rico with prompt and decisive public health actions. Some of these include (1) establish hepatitis C prevention as a priority for state and municipal public health authorities, (2) raise awareness and educate target populations about HCV transmission and prevention, (3) increase clinician awareness of the HCV reporting system and the epidemiology and management of hepatitis C, (4) increase availability of diagnosis and treatment facilities, (5) increase access to effective drug treatment services, and (6) develop appropriate control measures to help reduce continued transmission in correctional settings.

Key words: Hepatitis C, Injection drug use, HIV, Public health actions.

Studies investigating the seroprevalence of hepatitis C virus (HCV) infection have been carried out in diverse populations, showing an estimated worldwide prevalence of 3% and a marked geographical variation, mainly attributed to the frequency and extent of its risk factors (1-2). A seroprevalence survey of HCV infection conducted in 2001-2002 among randomly selected adults aged 21 to 64 years residing in San Juan, Puerto Rico revealed that 6.3% (95% CI: 3.6%-10.9%) of individuals were positive for HCV antibodies (anti-HCV) (3). A significant ($p<0.05$) higher prevalence was observed among subjects with the following characteristics: age 30-49 years, male sex, 12 or fewer years of education, no health insurance coverage, lifetime heroin use, lifetime cocaine use, tattooing practices, history of imprisonment, and self-reported histories of hepatitis B virus infection and HIV/AIDS (Figure 1). Multivariate logistic regression revealed that tattooing practice (POR=8.9; 95% CI: 1.7-44.7), lifetime cocaine use (POR=5.5; 95% CI: 2.2-13.5), blood transfusions prior to 1992 (POR=4.0; 95% CI: 1.6-10.1), lifetime heroin use (POR=3.3; 95% CI: 1.4-7.8), and history of imprisonment (POR=2.3; 95% CI: 1.1-4.9) remained significantly ($p<0.05$) associated with HCV seropositivity. Data from the recent National Health and Nutrition Examination Survey (NHANES 1999-2002) indicated that the prevalence of anti-HCV in the United

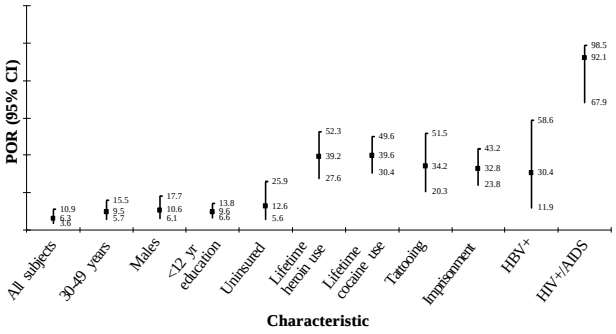

Figure 1. Weighted prevalence of HCV antibody according to selected characteristics in San Juan, Puerto Rico (n=964)

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States (US) ranged from 0.9% among adults aged 20-29 years to a peak of 4.3% in those aged 40-49 years (4). The large prevalence of HCV infection observed in Puerto Rican adults residing in San Juan suggests that HCV infection is an emerging public health concern that merits further investigation. Yet, prior serologic surveys carried out in allogeneic blood donors and women attending publicly funded prenatal clinics in San Juan have reported anti-HCV prevalence estimates within values comparable to those of the general US population (5-8). In this report we illustrate data that establish the need to start addressing HCV infection in Puerto Rico with prompt and decisive public health actions.

Puerto Rico still has a significant HIV/AIDS problem related to drug use.

HIV transmission in Puerto Rico parallels that of developing countries with intravenous drug injection transmission (49.3%) and heterosexual contact (25.2%) as the main exposure categories (9). In 2005, Puerto Rico ranked fifth in the reported rate of AIDS cases (26.4 per 100,000 population) compared with an overall rate of 14.0 per 100,000 in the US (10). San Juan, Puerto Rico continues to be one of the hardest hit regions, ranking eighth among all metropolitan statistical areas in the US (28.9 per 100,000 population in 2001). Therefore, the HIV/AIDS epidemic has not been controlled in the island and effective comprehensive disease containment measures have not been implemented.

A study that compared street-recruited drug users from Puerto Rico to Puerto Rican drug users from New York City found HIV seroincidence rates of 3.4 per 100 person-years in the Puerto Rico group and 0.9 in the New York group (11). The higher seroconversion rate found in Puerto Rico indicates a need to enhance HIV prevention efforts, including increasing methadone treatment and access to sterile syringes.

Prevalence of HIV and HCV infections among Puerto Rican drug users is very high.

Reyes and colleagues determined the prevalence of hepatitis C among 400 recruited injection drug users not in treatment living in Bayamón, Puerto Rico. This study revealed that the prevalence of anti-HCV was 89%, whereas the prevalence of HIV was 17% (12). In addition, 95.2% of HIV positive individuals were co-infected with HCV. Increasing years of injection, injecting in a shooting gallery, tattooing in prison, and self-reported STD infections were positively associated with HCV infection. Injection drug users who had initiated drug injection within the year prior to the study had a prevalence of HCV infection of 57%.

The greater percutaneous transmissibility of HCV compared with HIV explains the higher prevalence of HCV infection among injection drug users observed in this study - it has been estimated that HCV is nearly 10 times more infectious than HIV by percutaneous blood exposure to small volumes of blood (13). These data underscore the need to develop prevention programs aggressively targeting this group of initiators to significantly reduce their risk of infection and the risk to others.

Studies have shown that frequency of injection has been consistently higher among Puerto Rican injection drug users than among other groups of injection drug users, and that drug injection in Puerto Rico often occurs in high risk settings in which sterile injecting equipment and cleaning materials are scarce (14-18). For example, Colón and colleagues reported that the mean frequency of injection among injection drug users in East Harlem and Puerto Rico was 2.8 and 5.4, respectively (16). Deren and colleagues have also reported higher levels of needle-sharing behaviors in Puerto Rico compared to New York (15).

Various researchers have suggested that differences in high-risk behaviors among Puerto Rican injection drug users who reside in Puerto Rico compared with those who reside in New York City may be partially explained by differences in structural factors, including much greater availability of needle exchange programs and drug treatment programs, greater ease of getting into methadone maintenance treatment programs and larger healthcare utilization for those living in New York City (19-21). In spite of the evidence supporting the role of drug treatment in HIV prevention and recommendations of the NIH Consensus Statement on Management of Hepatitis C to institute measures to reduce transmission of HCV among injection drug users (22-23), a study of availability of drug treatment services in Puerto Rico revealed a 34.7% reduction in total treatment capacity from 1998 to 2002 even though need for treatment had not decreased (24).

Prevalence of hepatitis C infection is elevated among prison inmates in Puerto Rico.

HCV infection rates are alarmingly high in inmate populations, mainly attributed to injection drug use and sharing of injection equipment (25-29). Considering that the rate of incarceration in prison in Puerto Rico at year-end 2005 was 293 per 100,000 population (30) and the high-risk behaviors among Puerto Rican injection drug users, one would expect a high prevalence of hepatitis C infection in this population.

A seroprevalence study conducted among the correctional inmate population in Puerto Rico during 1998 revealed that the prevalence of hepatitis C infection among 11,530 inmates who volunteered for hepatitis C testing

was 49.3% (31). The majority of seropositive individuals were males aged 20-29 years (49%) and 30-39 years (36.7%) who reported a history of tattooing practices (80.1%) and injection drug use (68%). Of 5,686 HCV seropositive inmates, 10.5% were co-infected with HIV. Albizu and colleagues recently conducted a study to address the needs for drug abuse/dependence treatment and prevention for HIV, HCV and HBV infections among inmates of Puerto Rico's prison system (32). Based on a random sample of 1,179 inmates, 26.9% self-reported a diagnosis of HCV infection. After adjusting for age, sex and number of years in prison, HCV was significantly associated with tattooing practices outside prison (POR=2.0; 95% CI: 1.13-3.60) and inside prison (POR=3.68; 95% CI: 2.17-6.25). Injection drug use was also associated with practices outside prison (POR=13.81; 95% CI: 9.16-20.82) and inside prison (POR=11.19; 95% CI: 5.91-21.17). These results are consistent with a higher prevalence of HCV infection in prison populations than in the general population and underscore the need of implementing evidence-based measures to protect both the health of the inmate population and their communities.

Knowledge of HCV infection in the general population is limited.

Primary prevention of HAV and HBV can be achieved by vaccination; however, HCV infection can only be reduced through behavioral interventions to reduce risk factors for infection. A comprehensive health survey conducted in the US revealed that a substantial proportion of adults are either uncertain or inaccurately informed about HCV infection, and that racial differences in knowledge may exist (33). Although Blacks were more likely to report having heard of HCV than Whites or Hispanics (94% vs. 89% and 87%, respectively, $p<0.05$), Blacks were less likely to respond accurately to multiple statements regarding HCV risks and prevention.

As part of an epidemiological study to estimate the prevalence of anti-HCV in Puerto Rico, a scale of eight items (four related to HCV transmission, one to HCV prevention, and three about HCV clinical sequelae) was used to assess the level of knowledge of hepatitis C among adults (34). The percent of participants with correct responses fluctuated from 0.6% to 34.4%. The average score of correct responses was 3.6±1.1. Only 20.1% of the participants had appropriate knowledge, defined as 5 (70%) correct responses or more. Although the vast majority of individuals were aware that drug injection is the main route of HCV transmission, 78.9% reported that HCV is vaccine-preventable, and only 1.8% mentioned that HCV infection can cause liver damage. HCV average summary knowledge scores significantly ($p<0.05$) differed by age, education level, annual family income, health coverage and level of HCV counseling received.

Adults in this study demonstrated an inadequate level of knowledge about HCV infection, especially in the areas of transmission and prevention. Health care providers, health educators, and other community-based organizations must play an active role in raising awareness and educating target populations about HCV infection. Efforts to educate the public and health professionals about prevention and control of HCV infection in Puerto Rico are needed. These should include the development of a comprehensive education initiative to increase awareness among the general public and access to prevention materials among high-risk populations.

Morbidity and mortality among HIV patients co-infected with HCV is higher than in mono-infected HIV patients.

Co-infection with HIV and HCV is common because risk factors for transmission are similar. HCV prevalence among HIV patients averages 40% in the US and Europe and may exceed 80% among injection drug users (35,36). Accumulating evidence suggests that HIV accelerates the natural course of chronic HCV infection leading to increased risk of cirrhosis, hepatocellular carcinoma and decompensated liver disease, while other studies suggest that HCV coinfection may accelerate the course of HIV disease (35, 37-38). On the other hand, deaths from liver-related mortality in co-infected patients are expected to increase due to the wide availability of highly active antiretroviral therapy (39).

Evaluation of the morbidity and mortality experience in a cohort of 356 HIV patients in Bayamón, Puerto Rico between 1998 and 2000 revealed that the prevalence of HCV was 54% in the overall cohort and 81% in injection drug users (37). Although mortality rates were similar in patients with and without HCV infection (57.7% versus 51.1%, respectively, $p>0.05$), a significant higher proportion of HIV-HCV co-infected patients died of liver damage (hepatic dysfunction, cirrhosis or hepatic failure) compared to HIV mono-infected patients (19.6% versus 1.4%, respectively, $p<0.01$). These findings underscore the impact of HCV infection in the HIV epidemic.

Chronic hepatitis C in Puerto Rican patients might have worse prognosis.

A distinct characteristic of HCV is its tendency to cause chronic liver disease, with nearly 75%-85% of patients developing chronic infection (23). It has been estimated that at least 20% of chronic HCV patients develop cirrhosis, end-stage liver disease and liver cancer. HCV is the cause of about half of the cases of primary liver cancer in the developed world.

At the present time, the optimal regimen appears to be a 24- or 48-week course of the combination of pegylated alpha interferon and ribavirin (23). However, earlier studies have shown that the HCV genotype affects virologic response after interferon alpha treatment. Patients with genotypes 2 and 3 are two to three times more likely to respond to interferon-based therapy than patients with genotype 1.

What do we know about the clinical manifestations of Puerto Rican HCV patients? Among 332 HCV patients evaluated at the University of Puerto Rico Clinics from 1990 through 2001, more than half (51.2%) presented fibrosis and 31% cirrhosis (40). Of 557 patients referred to the University of Puerto Rico Liver Transplant Clinic from 1999 to 2005, HCV was the main etiology of liver disease in 50.4% of the cases. Rodríguez and colleagues (41) documented that 77% of 500 patients with chronic HCV infection evaluated by gastroenterologists at private practices in Puerto Rico had genotype 1. The response to combination therapy of interferon alfa 2-b plus ribavirin in patients with chronic hepatitis C was evaluated in a sample of 210 patients (42). Sustained viral response was 23% in naïve patients, 45% in relapsers previously treated with interferon, and 8% in non-responders to interferon. These findings are consistent with previous studies that have documented a lower sustained virologic response among Hispanic patients (43-44).

It is time to start addressing the challenges of HCV infection with public health actions.

An island-wide survey is being conducted to estimate the prevalence of anti-HCV, assess patterns of co-infections (HIV, HAV, HBV, HSV-2, HPV-16, and HPV-18), and evaluate risk factors for HCV for the Puerto Rico household, adult population (34). These data will provide further information to guide prevention efforts.

Nevertheless, there are immediate actions that can be implemented based on the information at hand to start addressing the challenges of HCV infection in the foreseeable future (23, 45). These public health strategies include: (1) establish hepatitis C prevention as a priority for state and municipal public health authorities, (2) raise awareness and educate target populations about HCV transmission and prevention, (3) increase clinician awareness of HCV mandatory reporting system and the epidemiology and management of hepatitis C, (4) increase availability of diagnosis and treatment facilities, (5) increase access to effective drug treatment services, and (6) develop appropriate control measures to help reduce continued transmission in correctional settings. These recommendations are consistent with the framework provided by the Centers for Disease Control and Prevention and the National Institutes of Health Consensus Development Conferences on the Management of Hepatitis C (23,46).

Moreover, in an effort to develop a public health response to HCV infection in the US, the *Hepatitis C Epidemic Control and Prevention Act* was introduced to the Senate (S. 1445) and House of Representatives (H.R. 2552) of the US Congress "to amend the Public Health Service Act to direct the Secretary of Health and Human Services to establish, promote, and support a comprehensive prevention, research, and medical management referral program for hepatitis C virus infection" (47,48). The development of a public health policy advocacy plan of action would contribute to increase awareness of HCV and its sequelae in order to improve prevention and control efforts. As Sir Austin Bradford Hill stated in 1965, "Incomplete scientific evidence does not confer upon us the freedom to ignore the knowledge we already have, or to postpone the action that it appears to demand" (49).

Resumen

Estudios que han investigado la seroprevalencia de la infección con el virus de la hepatitis C (VHC) han estimado una prevalencia global de 3%. Un estudio realizado en una muestra aleatoria de viviendas en el municipio de San Juan reveló que 6.3% de los adultos entre 21 y 64 años tenía evidencia de anticuerpos contra el VHC. Estos datos sugieren que los puertorriqueños tienen una prevalencia mayor de anticuerpos para el VHC que la observada en la población adulta de los Estados Unidos (0.9%-4.3%). Este artículo resume la evidencia acumulada de diversas investigaciones que establece la necesidad de abordar la problemática de esta infección desde una perspectiva de salud pública incluyendo las medidas siguientes: (1) lograr que las autoridades estatales y municipales establezcan la prevención de la hepatitis C como una prioridad de salud pública, (2) aumentar la concienciación y la educación sobre la transmisión y la prevención del VHC en la población general y las poblaciones de alto riesgo, (3) aumentar el conocimiento de los profesionales de la salud sobre la notificación obligatoria de la hepatitis C y la epidemiología y el manejo de la enfermedad, (4) aumentar la disponibilidad de facilidades para el diagnóstico y el tratamiento de la hepatitis C, (5) aumentar el acceso a servicios de tratamientos efectivos para la drogodependencia y (6) desarrollar medidas de control adecuadas para reducir la transmisión del VHC en el sistema correccional de Puerto Rico.

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