



Case-Reporting of Acute Hepatitis B and C Among Injection Drug Users

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ABSTRACT *Although public health surveillance system data are widely used to describe the epidemiology of communicable disease, occurrence of hepatitis B and C virus (HBV and HCV, respectively) infections may be misrepresented by under-reporting in injection drug users (IDUs). This study was carried out to examine the relationship between HBV and HCV incidence and case-reporting of hepatitis B and C in Seattle IDUs. Names of participants in a Seattle IDU cohort study who acquired HBV or HCV infection over a 12-month follow-up period were compared to a database of persons with acute hepatitis B and C reported to the health department surveillance unit over the same period. Of 2,208 IDUs enrolled in the cohort who completed a follow-up visit, 63/759 acquired HBV infection, 53/317 acquired HCV infection, and 3 subjects acquired both HBV and HCV. Of 113 cohort subjects who acquired HBV or HCV, only 2 (1.5%) cases were reported; both had acute hepatitis B. The upper 95% confidence limit for case-reporting of hepatitis C in the cohort was 5.7%, and for hepatitis B, it was 7.5%. In this study, reporting of acute hepatitis in IDUs was extremely low, raising questions regarding the use of community surveillance data to estimate underlying incidence in that population group.*

KEYWORDS *Hepatitis B, Hepatitis C, Substance use, Surveillance.*

INTRODUCTION

Hepatitis B and C are among the serious illnesses from blood-borne viruses that injection drug users (IDUs) may acquire over their drug use career.¹ High prevalence of antibody to hepatitis B virus (HBV) and hepatitis C virus (HCV) has been reported from cohort and cross-sectional studies of IDUs in the United States, Europe, and Australia,² with HCV antibody (anti-HCV) prevalence between 65% and 90% and prevalence of core antibody to HBV (anti-HBc) 50%–90%. HCV incidence rates in IDUs vary between 10% and 30% per year and are generally 4 to 100 times higher than the incidence of HIV in the same population.^{3–6} HBV incidence in IDUs is somewhat lower, at 5%–10% per year.^{2–6}

Information about the epidemiology of hepatitis B and C in IDUs is also obtained from data on acute hepatitis cases reported to public health disease surveillance systems. In the sentinel hepatitis surveillance studies sponsored by the Centers

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for Disease Control and Prevention (CDC), 43% of acute hepatitis C in 1992–1995 and 13% of hepatitis B in 1990–1992 was associated with drug injection.^{7,8} There are several reasons to believe that disease surveillance systems may disproportionately undercount cases of hepatitis in IDUs. Medical care for IDUs may be sporadic, and clinic or emergency room visits may be reserved for serious illness.⁹ Moreover, only a minority of patients with acute hepatitis B may experience jaundice, and many cases may be either clinically inapparent or result in nonspecific illnesses.^{10,11} Similarly, only 25%–35% of acute hepatitis C cases are symptomatic, and few of these cases are icteric.¹² Mild and nonspecific manifestations of acute hepatitis may not lead to physician visits or diagnostic testing. Further, the manifestations of hepatitis in patients who are symptomatic may be similar to some symptoms of opiate withdrawal.¹³ Thus, drug users with acute hepatitis may not receive medical attention that could result in being diagnosed and reported to a disease surveillance program. In addition, drug user patients who are reported to surveillance programs may be reluctant to report illegal risk behavior to public health authorities, so that an unknown proportion of IDU cases could be attributed to another cause. Case data may also be incomplete on IDUs who are unable to be contacted because they are homeless or living in temporary housing. As a result, estimates of the burden of hepatitis borne by injection drug users may be extremely low. In this article, we evaluate reporting of hepatitis among IDUs in a cohort study who seroconverted to HBV- or HCV-antibody positive.

METHODS

Subjects and Data

The Risk Activity Variables, Epidemiology, and Networks (RAVEN) study is a longitudinal cohort study of blood-borne viral infections and risk behavior among IDUs living in Seattle, Washington. Eligibility criteria included injection of an illicit drug at least once during the previous 12 months, English or Spanish speaking, age 14 years or older, and not already enrolled in the study. Recruitment of eligible individuals occurred from June 1994 to May 1997 in nine locations in the Seattle area, including methadone drug treatment clinics, the county corrections facility, and a street outreach and social service agency located in an area of downtown Seattle in which drug buying and selling occurred. A random-numbers-based scheme was used to select the *n*th individual in each setting. Participants who were eligible and consented to enrollment were paid \$10 to complete the enrollment study visit and \$25 to complete the follow-up visit 1 year later. At each study visit, a standardized questionnaire was administered by a trained interviewer. A blood specimen was tested for anti-HCV and anti-HBc. Participants who were antibody negative at baseline were retested at the follow-up visit to detect seroconversions. HBV-negative IDUs were offered free hepatitis B vaccine; an evaluation of this effort to vaccinate study participants is in press.¹⁴ Study methods, including procedures for maximizing follow-up retention, are reported elsewhere in greater detail.^{5,15–17} All procedures involving human subjects were approved by two institutional review boards.

Viral Hepatitis Reporting in Seattle–King County

During the period that encompassed recruitment and follow-up of RAVEN subjects (June 1994 to May 1998), suspected or confirmed cases of acute hepatitis B and hepatitis C (non-A, non-B) were legally notifiable diseases under Washington State Administrative Code. Chronic cases of hepatitis B and C were not legally notifiable diseases.

The surveillance case definition for acute viral hepatitis requires satisfying both clinical and laboratory criteria. Clinical criteria included an acute illness with a discrete onset of symptoms and either jaundice or elevated serum aminotransferase levels. Laboratory criteria for acute hepatitis B included a positive immunoglobulin M core antibody to hepatitis B (IgM anti-HBc) or the presence of hepatitis B surface antigen (HBsAg) and the absence of IgM antibody to hepatitis A (IgM anti-HAV), if performed. If the patient was HBsAg positive, but did not meet clinical criteria, the case was considered to be a chronic hepatitis B infection. Laboratory criteria for acute hepatitis C included the absence of IgM anti-HAV, IgM anti-HBc, and HBsAg and the presence of anti-HCV or HCV RNA by the polymerase chain reaction.

Health care providers and laboratories reported by name the patients meeting these criteria to the Communicable Disease Epidemiology Section at Public Health—Seattle and King County (Public Health). Case report data included risk history (drug injection during the previous 6 months, multiple sex partners, transfusion of blood or blood products, etc.) and demographic, clinical, and laboratory data. For all suspected or confirmed hepatitis cases, public health staff attempted to locate the patient to complete a survey on onset of illness and risk factors and to make referrals for care.¹⁸

Matching RAVEN to Case Report Data

Three lists of RAVEN subjects (including name, alias, date of birth, gender, and race) were created. One list included RAVEN participants who seroconverted to anti-HCV or anti-HBc positive during the June 1994 to May 1998 study period; this list was compared against the January 1994 to December 1998 Public Health viral hepatitis surveillance database to obtain a count of the number of RAVEN seroconverters who were reported. Two other lists included a 50% random sample of RAVEN participants who remained anti-HCV or anti-HBc negative from enrollment throughout the follow-up period and a 50% random sample of RAVEN participants who were anti-HCV or anti-HBc negative at enrollment, but did not return for a follow-up. These lists were also compared against the public health database of acute hepatitis B and C cases to obtain an estimate of the proportion of study subjects in whom HBV or HCV seroconversion was not recorded.

To detect probable matches between the RAVEN lists and the public health database, study personnel used broadly inclusive criteria—surnames of public health cases were compared against the alphabetic listing of RAVEN names and aliases to detect any remotely similar names. We considered it a match between the RAVEN subjects lists and the public health database when a RAVEN name or alias was closely similar in spelling or pronunciation to the names in the public health database and gender was the same. Race, birth date, and gender were also compared against the public health database to detect any other possible matches, but no additional matches were found. The upper 95% confidence limit (CL) for the proportion of seroconverters who were reported to public health surveillance was calculated using standard methods and using methods appropriate when zero events are observed ($3/n$).¹⁸

RESULTS

Follow-up visits were completed with 2,208 of 2,977 individuals enrolled in the RAVEN study (74%). There were 1,153 RAVEN participants who were anti-HBc negative at baseline, 759 of whom completed follow-up (66%); 63 seroconverted

(cumulative annual incidence of 8.3%; Table 1). There were 538 RAVEN subjects who were anti-HCV negative at baseline, and 317 returned for follow-up (59%); 53 seroconversions were observed (cumulative annual incidence of 16.7%). There were three subjects who converted to both HBV and HCV positive. No matches were found among the sample of subjects lost to follow-up or among the sample of those who did complete follow-up, but for whom we did not observe any seroconversions. Of the 113 individual subjects who acquired HCV and/or HBV infection during follow-up, 2 were identified among reported cases (1.5% of all seroconverters). Both were HBV seroconverters reported to have acute hepatitis B (3.2% of all HBV seroconverters), and in both cases, drug injection was noted as the source of exposure. The upper 95% confidence limit for reporting of hepatitis C infection in our cohort was estimated¹⁸ to be 3/53 or 5.7%. For hepatitis B infection, the upper 95% confidence limit was 7.5%.

All subjects were asked at the follow-up interview whether they had been “sick with hepatitis” (having nausea, vomiting, diarrhea, or abdominal pain) or whether they had experienced jaundice (eyes or skin turning yellow, or urine is very dark). The wording was meant to detect awareness of symptoms that might reasonably prompt them to seek medical care. Of the subjects susceptible to HBV or HCV infection, 57 reported being “sick with hepatitis” during the follow-up period, including 17% of HBV seroconverters, 8% of HCV seroconverters, and 6% of subjects who did not seroconvert to either HBV or HCV ($P = .02$; Table 2). Of HBV seroconverters, 18% reported experiencing jaundice during follow-up versus 6% of HCV seroconverters and 4% of subjects who did not seroconvert ($P < .01$). Of the 53 HCV seroconverters, 4 reported either jaundice or other symptoms that could have led to seeking medical attention and possible case-reporting (7.5% of all seroconversions), and as mentioned, none of these was reported (Table 3). Of the HBV seroconverters, 14 were symptomatic (22%), and 2 were reported (14%).

DISCUSSION

In this study, very few IDUs who acquired HBV or HCV infection were reported to a public health hepatitis surveillance system, and this raises questions regarding

TABLE 1. Seattle RAVEN study injection drug using participants anti-HBc or anti-HCV negative at enrollment: study retention and seroconversion at 12 months and results of comparison to public health surveillance system database

	N	Lost to follow-up, n (%)	Retained, did not seroconvert	Seroconverted
At enrollment in RAVEN				
Anti-HBc negative	1,153	394 (34)	696	63
Anti-HCV negative	538	221 (41)	264	53
Number of RAVEN participants compared to Public Health database		220	432	113
Number of cases reported to Public Health		0	0	2

Anti-HBc, core antibody to hepatitis B virus; anti-HCV, hepatitis C virus antibody.

TABLE 2. Association between self-report of symptoms and seroconversion to HBV and HCV infection in Seattle RAVEN study injection drug users

	Seroconverted to:			No seroconversion, n (%)	P
	HBV and HCV, n (%)	HBV only, n (%)	HCV only, n (%)		
"Sick" with hepatitis					
Yes	0 (0)	10 (17)	4 (8)	43 (6)	.02
No	3 (100)	49 (83)	45 (92)	642 (94)	
Had jaundice					
Yes	0 (0)	11 (18)	3 (6)	30 (4)	<.01
No	3 (100)	49 (82)	46 (94)	662 (96)	

Note: Numbers may not sum to total because of missing data.
HBV, hepatitis B virus; HCV, hepatitis C virus.

the limitations of surveillance system data in characterizing viral hepatitis epidemiology among drug injectors. Indeed, because the majority of study participants who acquired HBV or HCV infection were apparently asymptomatic, they would not have met the CDC surveillance case definition. This suggests that alternate methods of hepatitis case-finding in IDUs may be needed to monitor hepatitis incidence in a community. However, even among those who were symptomatic and may have met the case definition, a relatively small proportion (14% of HBV converters and none of the HCV converters) was reported.

Potential reasons for under-reporting of IDUs with acute hepatitis include that IDU patients may not access the health care system for evaluation of symptoms and diagnoses or that symptoms of viral hepatitis are attributed to other causes, such as narcotic withdrawal. Because data on reporting of hepatitis infections in other at-risk groups were not obtained, it was not possible to determine whether under-reporting was more or less likely to occur in IDUs. Moreover, the sample of IDUs with symptoms of acute hepatitis was too small to study the relationship between acute disease and case-reporting in this population.

Other limitations to the study include that seroconverters in the cohort may have been reported under different names or aliases to the public health database. However, no matches were detected based on broad criteria of race, birth date, or gender. The proportion of seroconverters in this cohort who were reported to the surveillance unit was so low that it is unlikely that correction for the use of aliases would increase the proportion significantly. It is also possible that hepatitis report-

TABLE 3. Relationship among seroconversion, hepatitis symptoms, and case-reporting

	Seroconverters, N	Symptomatic/ seroconverters (%)	Reported cases/ symptomatic (%)
HBV	63	14/63 (22.2)	2/14 (14.3)
HCV	53	4/53 (7.5)	0/4 (0)

HBV, hepatitis B virus; HCV, hepatitis C virus.

ing in Seattle–King County is lower than the US average, but this is also unlikely because procedures for case-finding are similar to those used in other regions of the United States. In fact, hepatitis B incidence in King County for 1994–1998 was similar to that in other counties in Washington State and in the United States.^{19,20} Some of the cohort members classified as seroconverters may have had false-positive test results, but this would have led to only a few subjects being erroneously included in the denominator of the reporting rate.^{21,22} In addition, data on access to health care were not collected in this study, and data on whether seroconverters sought care for symptoms potentially related to hepatitis were not ascertained.

Strengths of the study include the broad sampling frame for the cohort, the number of seroconversions observed, and efforts to determine whether there were seroconverters among those lost to follow-up or if we failed to detect infection among subjects who did not meet our criteria for seroconversion.

There have been very few studies evaluating the relationship between incidence of infection and hepatitis case-reporting systems. One study of under-reporting of hepatitis in the US CDC hepatitis sentinel counties compared passive reporting in 1980–1983 to a stimulated reporting system implemented in 1984 that included prompts to physician offices, hospital infection control staff, laboratory directors, and the medical society.²³ During stimulated reporting, there was no increase in the number or proportion of hepatitis B or non-A, non-B cases among IDUs; rather, their proportion among all cases decreased as reporting among gay and bisexual men increased. An overall increase in viral hepatitis reporting during the active surveillance period led to the estimate that passive reporting of hepatitis in US populations was approximately 65% complete. Although passive reporting in a sentinel county may be higher than in other areas, the estimate of 65% completeness is more than six times the 95% upper confidence limits of 8% reporting for HBV and 6% for HCV infections found in our study. Our estimates were also somewhat lower than (but more similar to) those obtained by Crofts et al.,²⁴ which showed that only 12% of HCV infections in IDUs are reported in Australia. Their estimate was obtained by relating the cumulative number of reported hepatitis cases to the estimated number of HCV-positive IDUs in Australia. Our data also suggest that, for hepatitis B virus infections, the small proportion who experience any symptoms (22%) may reduce the likelihood of case-reporting, and that for HCV, the relationship between acute infection and case-reporting is further attenuated by the very low proportion who experience the hepatitis syndrome (8%).

Together, these data suggest that dependence of routine communicable disease surveillance systems on both access to clinical services and individual clinicians' reporting behavior may lead to under-representation of IDUs among hepatitis cases, particularly in the case of hepatitis C virus infection. To the degree that surveillance system data are used to estimate the relative burden of hepatitis disease borne by drug injectors, there may be underallocation of prevention and care resources.

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