

Results of Universal Prenatal Screening for Hepatitis C Infection in a Remote American Indian Primary Care Population

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ABSTRACT

BACKGROUND: Although chronic liver disease remains a major area of health disparity for American Indian (AI) people, the epidemiology of hepatitis C virus (HCV) infection among AI people is poorly documented. Because of suspected high local prevalence, two remote AI clinics in the Northern Plains implemented universal prenatal HCV screening in 2005. When this screening program reported an unexpectedly high prenatal anti-HCV (anti-HCV antibody) positivity rate, we conducted a case-control study to determine risks for infection and opportunities for community intervention.

MAIN FINDINGS: The clinics screened a total of 205 pregnant women (median age, 22 years). Of these 205 women, a total of 13 (6.3%; 95% confidence interval, 3.4–10.6) had anti-HCV confirmed. Of the anti-HCV-positive women, 10 (76.9%) were aged 15–24 years. We included 10 cases and 40 anti-HCV-negative prenatal controls in a case-control study. On multivariate analysis, only injection-drug use (IDU) remained associated with HCV seropositivity.

CONCLUSIONS: Universal prenatal screening revealed a high prevalence of anti-HCV at these remote AI clinics. This population has not been previously described at being at elevated risk for HCV infection. In order to reduce health disparities, young, rural AI populations seeking prenatal care need to be included in interventions to reduce HCV transmission.

Key Words: American Indians; hepatitis C, infection; prenatal; intravenous drug use; rural

INTRODUCTION

A total of 4.1 million U.S. residents, or 1.6% of the population, has ever been infected with hepatitis C virus (HCV). Of them, 3.2 million, or 80%, are chronically infected (Armstrong et al., 2006). The national prevalence of HCV infection among women of childbearing age is approximately 1%, corresponding to an estimated 40,000 births to HCV-positive women each year (Armstrong et al., 2006). In the United States, HCV is spread chiefly by injection-drug use (IDU), which accounts for 60%–80% of infections (Wang et al., 2007). Prenatal HCV testing is only recommended for women with HCV risk factors (Alter, Kuhnert, & Finelli, 2003), such as a history of injection-drug use or blood/blood product transfusion. Universal prenatal HCV testing is not recommended by the Centers for Disease Control and Prevention (CDC) chiefly because the likelihood of vertical transmission is low (5%–6%) (Centers for Disease Control and Prevention [CDC], 1998).

In July 2005, an Indian Health Service (IHS) prenatal care provider instituted universal prenatal HCV testing (regardless of risk factors) in two IHS clinics in a rural area of the Northern Plains (Montana, Wyoming, and North and South Dakota) where frequent drug use, most notably with methamphetamine and opiates, had been suspected but not documented. Specific population-based data on local injection drug use patterns, and the health-seeking behavior of persons who use them, have not been available for American Indian and Alaska Native (AI/AN) people in this part of the United States. IHS is the federal agency responsible for health care for eligible AI/ANs. In July 2006, the IHS Division of Epidemiology and Disease Prevention was notified by these clinics of a apparently high number of positive prenatal HCV test results among the population seeking prenatal care at these clinics. A field investigation was begun in August 2006 by IHS.

Objectives of the investigation were to confirm the positive prenatal HCV testing results, to estimate the prevalence of antibodies to HCV (anti-HCV), to identify risk factors associated with HCV infection, and to provide recommendations to IHS and the Tribal Health Department to prevent further HCV infections among this population.

METHODS

Human Subjects

The Centers for Disease Control and Prevention and IHS determined that this field investigation was exempt from full Institutional Review Board review. The study was implemented in collaboration with the local Tribal Health Department as a community-based, participatory public health investigation.

Setting

We conducted this investigation at two AI clinical facilities serving remote AI communities in the Northern Plains of the United States. In order to respect local preferences regarding community confidentiality, the specific setting of the investigation will remain confidential.

Prevalence study

For case finding, we used the Resource and Patient Management System (RPMS), an electronic clinical and administrative data software system developed by IHS. At each clinic, we also reviewed medical records and consulted IHS and reference laboratory records. We defined a case of hepatitis C infection, past or current, as the presence of anti-HCV antibodies by enzyme immunoassay (EIA), confirmed by either recombinant immunoblot assay (RIBA® [Chiron Corporation, Emeryville, California]) for anti-HCV (past or current infection) or by nucleic acid testing (NAT) for HCV RNA (current infection) (Alter et al., 2003), in a woman with a first prenatal consultation in either of the two

IHS clinics during July 1, 2005–July 31, 2006. Prenatal anti-HCV prevalence was calculated by dividing the number of pregnant women with confirmed past or current HCV infection by the number of pregnant women who had a first prenatal consultation during the study period and who were screened for HCV infection. Overall and age-specific prevalence estimates were calculated with exact 95% confidence intervals (CI) based on a binomial distribution.

Case-control Study

Subsequently, we conducted an unmatched case-control study to identify risk factors associated with HCV infection. Our case definition for the case-control study was the same as for the prevalence study. First, we randomly selected four control subjects per case-patient from women who attended either of the IHS clinics for their prenatal care and whose prenatal anti-HCV antibody by EIA was negative during the study period. Second, we made up to five attempts to contact each case-patient and selected control subjects by telephone to obtain their oral consent to participate to the study. Third, we asked respondents to complete a standardized questionnaire either at their domicile, or by phone or at the clinics. The questionnaire for HCV infection risk factors included questions on blood/blood product transfusion, solid organ transplant, health-care exposure, occupational exposure, multiple sex partners, sexual intercourse with an infected partner, tattoos, incarceration, drug use, and IDU. We asked respondents about exposures that occurred before the pregnancy during which case-patients and control subjects were screened by using a calendar to help them recall dates.

Data Analysis

Only one and two variable models were considered because of limited sample size. Stata® 10/SE for Windows (College Station, Texas, USA) was used to do exact analyses.

RESULTS

A total of 259 women had a first prenatal consultation at one of the two clinics during the study period. Of them, 205 (79.1%) were screened for HCV infection (median age, 22; range, 13–40). The majority of unscreened women had chosen to seek prenatal care or had been referred to another health-care facility by IHS. Anti-HCV antibodies were detected by EIA in samples from 17 screened women (17/205; 8.3%). A confirmatory RIBA test was requested by treating clinicians for 15 EIA-positive women; no NATs were requested. Two RIBA tests were negative, and 13 confirmed the presence of anti-HCV antibodies. Case patients' median age was 23 (range, 19–29 years). The overall prevalence, therefore, of confirmed anti-HCV antibody was 6.3%, with the highest age-specific prevalence (7.4%) identified in the 15–24-year age category (Table 1).

Table 1. Prevalence of hepatitis C virus seropositivity among pregnant American Indian women by age group — Northern Plains, 2005–2006

Age (yrs)	Tested (n)	RIBA®-positive (n)	Prevalence (%)	95% CI
<15	3	0	0	0–70.8
15–24	136	10	7.4	3.6–13.1
25–34	57	3	5.3	1.1–14.6
35–44	9	0	0	0–33.6
Overall	205	13	6.3	3.4–10.6

Note. RIBA, recombinant immunoblot assay; CI, confidence interval.

Thirteen (13/15; 87%) case-patients were successfully contacted. Of those patients, three refused to participate; therefore, our case-control study included 10 case-patients and 40 control subjects. Control subjects' median age was not different from case-patients' (23 years; range, 16–34 years). In Table 2, we present odds ratios (OR) for risk factors associated with HCV seropositivity. In the univariate analysis HCV seropositivity was strongly associated with IDU before pregnancy (OR, 200.0; 95% CI, 22.7 – infinity; p -value < 0.001), and with illicit drug use, sex with an HCV-positive partner, use of methamphetamine, and having had six or more sexual partners before pregnancy. Therefore, all of the multivariate logistic models we subsequently fit included IDU and one other risk factor associated with HCV seropositivity in the univariate analysis. HCV seropositivity was not associated with blood/blood product transfusion, solid organ transplant, health-care exposure, occupational exposure, tattoos, and incarceration. Ever having used illicit drugs, having sex with HCV-positive partner, methamphetamine use, and having had six or more sex partners did not remain associated with HCV seropositivity after adjusting for IDU, indicating strong confounding.

DISCUSSION

This is the first report to describe anti-HCV prevalence and risk factors associated with HCV seropositivity in prenatal patients from a rural AI population. The prenatal confirmed anti-HCV antibody prevalence (6.3%) described in this report was six times higher than the prevalence among women of childbearing age in the U.S. population (Armstrong et al., 2006). The strongest risk factor for HCV seropositivity was IDU before pregnancy. These results represent an important step toward investigating and understanding the nature of HCV risk for AI women.

Because data are generally lacking in regard to HCV infection prevalence among AI/AN people, our work adds significantly to the body of work in this population. The most directly comparable work is a 2004 study among an urban AI population that reported results of universal prenatal anti-HCV testing. The overall prevalence of positive anti-HCV EIA in that study was 3.1% (Wilson, 2004). As opposed to our results, the trend in that study was toward increasing anti-HCV prevalence with increasing age. In a population-based study in Alaska, the minimum HCV infection prevalence estimate among ANs was 0.81% among those aged 20–39 years and 0.88% among females (McMahon et al., 2004). Our investigation reported a higher HCV infection prevalence than either of these studies.

Clearly, the population of rural Americans with a history of IDU is one that is crucial to include in public health interventions designed to reduce HCV-associated health disparities. We identified IDU before pregnancy as the primary risk factor for HCV infection. All other risk factors associated with HCV infection in the univariate analysis, e.g. ≥ 6 sexual partners before pregnancy, were not associated after controlling for IDU. Other studies have reported IDU as the most important risk factor for HCV transmission even among a population with high sexual risks (McMahon, Pouget, & Tortu, 2007). IDU has been reported as the strongest risk factor for HCV infection among the general U.S. population (Armstrong et al., 2006), among U.S. blood donors (Murphy et al., 2000), and in an HCV prospective screening study in an urban AI clinic (Neumeister et al., 2007). In a recent publication, pregnancy hospitalizations with a diagnosis of amphetamine abuse had doubled during 1998–2004 and were most frequent among rural women aged < 24 years living in the western United States (Cox, Posner, Kourtis, & Jamieson, 2008), which is similar to the population in which we conducted our work. We identified lifetime methamphetamine use reported by 67% of case-patients and 13% of control subjects (Table 2).

Table 2. Risk factors for hepatitis C virus seropositivity among pregnant American Indian women — Northern Plains, 2005–2006

	Cases	Control	Unadjusted	Risk factors adjusted by IDU*	IDU adjusted by risk factors*
	n/N (%)	n/N (%)	OR (exact 95% CI)	OR (exact 95% CI)	OR (exact 95% CI)
IDU	8/9 ^a (89)	0/40 (0)	200.0 (22.7–inf)	--	--
Ever used any illicit drugs	9/9 (100)	8/40 (20)	42.8 (6.0–inf)	3.6 (0.1–inf)	39.2 (4.1–inf)
Sex with HCV-positive partner	4/9 (44)	1/39 (3)	6.2 (1.3–46.3)	5.8 (0–38.5)	74.4 (7.5–inf)
Ever used methamphetamine	6/9 (67)	5/40 (13)	12.9 (2.0–107.3)	7.2 (0–280.8)	83.4 (9.6–inf)
≥6 sex partners	8/10 ^b (80)	11/38 ^b (29)	9.3 (1.5–103.6)	2.2 (0.1–inf)	84.2 (9.8–inf)

Note. Cases, case-patients; Controls, control subjects; OR, odds ratio; CI, confidence interval; IDU, injection drug use; inf, infinity.

*Four separate models were constructed, each model includes IDU and one risk factor

^aOne case-patient refused to answer questions related to illicit drug use.

^bTwo control subjects refused to answer questions related to sexual behavior.

A high prevalence of anti-HCV antibodies was identified in this study because universal prenatal HCV testing was implemented. However, universal HCV testing in pregnancy has been demonstrated not to be cost-effective, and is therefore not a standard of care (Plunkett & Grobman, 2005). In the long-term, a standard HCV infection risk assessment, together with counseling, might be a more effective strategy to identify women at risk for HCV infection in this rural community. This approach might avoid unnecessary anxiety for women without risk factors. Conversely, because of the suspected high rate of IDU among this population and the risk for IDU underreporting (Magura & Kang 1996), a standard HCV infection risk assessment might miss a substantial number of patients at high risk among this prenatal population.

Confirmation of positive anti-HCV EIA by HCV NAT and genotyping of HCV were not performed by the treating clinicians in the patients reviewed in this investigation. Since 20–30% of those testing antibody positive might be expected to clear the virus and only those chronically infected (i.e. NAT positive) can transmit the virus, this information is important to inform women about the risk of vertical transmission. Similarly, HCV genotype results can provide patients and providers with valuable information on the likelihood of responding to antiretroviral therapy (Hoofnagle & Seeff, 2006). Incomplete workup of AI/AN patients diagnosed with HCV infection has been documented in other settings, and is thought to relate to lack of treatment resources (Norton, Redd, & Bryan, 2009).

The major strength of our study is that it was conducted using clinical data, available both in paper charts and in a robust electronic data system (RPMS), from a rural population with universal access to primary health care. Our findings are, however, subject to certain limitations. First, our sample size was limited by the size of the population served by the two prenatal clinics, and the setting of only two clinics in a specific geographical region limits our ability to generalize study results to other AI groups. Second, studies of volunteer blood donors have reported that 30%–50% of those with an HCV-positive screening admitted to a history of IDU after being presented with their result. None of these donors had reported this risk factor at the time of donation (Orton, Stramer, Dodd & Alter, 2004). In our study, all case-patients (who knew about their seropositivity) reported IDU, but none of the control subjects did, raising the question of underreporting of IDU among

the control subject group. This might have overestimated the association between IDU and HCV infection. Third, during the study period, HCV NATs were not requested as either confirmatory tests (Alter et al., 2003) or as part of the standard hepatitis C workup. Therefore, we cannot report on the proportion of patients who were HCV RNA-positive.

CONCLUSION

Our discovery of a high prevalence of prenatal HCV infection represents a challenge to providers of prenatal and general medical care, particularly in this isolated AI population with existing health disparities and behavioral risk factors (Mahoney & Michalek, 1998). Both IHS clinics involved in this investigation have added an IDU assessment to standard patient intake to help identify patients who should be screened for HCV infection. In addition, the Tribal Health Department, in coordination with the local IHS clinics, has been active in encouraging tribal members with a history of IDU to obtain HCV screening. Prevention activities to reduce HCV transmission through IDU need to include access to testing and counseling services and drug treatment. Special programs have been developed to address the challenge of delivering HCV infection treatment to populations who have limited access to specialty care (Arora, Thornton, Jenusky, Parish & Scaletti, 2007), meaning that although the patients identified in this screening programs face substantial barriers to treatment, such treatment has been successfully delivered to rural Americans, including AI/AN people. These programs may be complicated by the difficulty of providing HCV treatment to intravenous drug users with limited eligibility criteria (Hagan et al, 2006). Continued investigation is needed in rural AI and non-AI populations to evaluate HCV prevalence and the contribution of IDU to HCV infection, and to guide prevention measures that are appropriate for the specific communities affected. Providers of rural health care should, like other providers, perform an accurate and complete assessment of behavioral health risks, and refer patients with behavioral risks for appropriate testing and treatment.

DISCLAIMERS

(1) Use of trade names is for informational purposes only and does not constitute endorsement by the Centers for Disease Control and Prevention or the Indian Health Service.

(2) The findings and conclusions of this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention or the Indian Health Service.

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