



Hepatitis C Diagnoses in an American Indian Primary Care Population

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ABSTRACT

BACKGROUND: Despite large disparities in the burden of chronic liver disease, data on hepatitis C virus (HCV) infection among American Indians (AIs) are lacking. We reviewed hepatitis C diagnoses in 35,712 AI/AN primary care patients. **MAIN FINDINGS:** At least one HCV-associated ICD-9 code was recorded in 251 (1%) patients between October 1, 2001 and September 30, 2003. An HCV enzyme-linked immunoassay (HCV-EIA) was sent in 209 (83.0%); 206/209 (99%) were positive. Confirmatory testing was performed in 144/206 (70%) HCV-EIA positive patients; HCV infection was confirmed in 144 (100%). In the 90/144 (63%) charts with risk factor documentation, injection drug use was the most common risk factor (61/90, 68%). Deficiencies were present in hepatitis B and HIV testing, and hepatitis A and B vaccination. **PRINCIPAL CONCLUSIONS:** Improvements in laboratory workup of HCV and co-infections, risk factor ascertainment and documentation, and adult vaccination are needed to address HCV effectively in this population.

Key Words: Community/public health; Infectious Disease; Special population: Native American/First Nations; Primary Care Issues

INTRODUCTION

Chronic liver disease (CLD) represents a major area of health disparity for American Indians and Alaska Natives (AI/ANs), in whom the age-adjusted CLD mortality rate is more than twice that of other racial groups. 1 In a recent Centers for Disease Control and Prevention (CDC)/Indian Health Service (IHS) study, approximately 5.5% of all adult AI/AN users at two IHS sites had CLD, of which approximately one quarter was caused by hepatitis C or hepatitis C plus alcohol abuse. 2

In the United States, hepatitis C virus (HCV) infection accounts for approximately 40% of chronic liver disease (CLD). 3,4 Major risk factors for HCV infection include injection drug use (IDU), receipt of clotting factors prior to 1987, and receipt of blood or solid organs before 1992. 5-9 Given the burden

of CLD in AI/AN populations, determining gaps in HCV diagnosis and disease management in AI/ANs is essential to improving outcomes and allocating resources for prevention and treatment.

We undertook this study to: 1) characterize diagnoses of HCV infection in a well-defined primary care IHS AI/AN population; 2) determine the completeness of HCV-related patient evaluation and treatment; and 3) identify aspects of HCV-related patient care in need of improvement.

METHODS

Human Subjects: This project was reviewed/approved by institutional review boards of the Indian Health Service, Centers for Disease Control and Prevention, and the University of New Mexico Health Sciences Center. Approval was also obtained from the involved IHS Service Unit Health Boards.

Setting: We performed our study at two IHS clinical facilities (service units) in the southwestern United States.

Subjects: Using the IHS electronic medical record system, we searched for patients who met all of the following criteria: 1) The patient was an AI/AN aged 18 years or older as of the beginning of the study period (October 1, 2001 through September 30, 2003); (2) the patient had > 1 in-patient admission(s) or out-patient visit(s) to an IHS facility during the study period; (3) for at least one admission or visit during the study period, or within three years prior to the beginning of the study period, the patient was assigned a HCV-related International Classification of Diseases, Version 9 (ICD-9) diagnosis (Appendix A). We considered confirmed case-patients to be those whose laboratory results indicated infection with HCV, defined as: (1) HCV enzyme immunoassay (EIA) antibody positive plus one or more confirmatory test (recombinant immunoblot assay [RIBA] or HCV nucleic antibody test [NAT]) positive; or (2) In the absence of confirmatory testing, EIA antibody positive with signal-to-cutoff ratio ≥ 3.8 .

We extracted the following patient information by electronic medical record and paper chart review:

Demographic data: date of birth, sex, and tribal affiliation.

HCV laboratory tests: HCV EIA, including signal-to-cutoff ratio (if available), HCV antibody RIBA, HCV genotype, HCV polymerase chain reaction (PCR) qualitative, and HCV ribonucleic acid (RNA) quantitative.

Past or present co-infections: hepatitis A, B, and D antibodies; HIV antibody.

Additional tests: alanine aminotransferase [ALT], liver ultrasound and computerized tomography, liver biopsy.

Additional CLD-related diagnoses or co-morbid conditions: alcoholic liver disease, non-alcoholic steatohepatitis, other non-infectious causes of hepatitis and/or chronic liver disease, diabetes mellitus, hepatocellular carcinoma.

Treatment and vaccination history: HCV treatment, hepatitis A/B vaccination history.

Risk factors for HCV infection: history of injecting drug use, blood or blood product transfusion or whole organ transplantation prior to 1992, and receipt of clotting factors prior to 1987.

Data Analysis: Analysis was performed using Epi-Info 3.3.2 (Centers for Disease Control and Prevention, Atlanta, Georgia), Excel (Microsoft, Redmond, Washington) and JMP 5.0 (SAS Institute, Cary, North Carolina). Continuous variables were tested using the t-test for means with unequal sample sizes and assumption of equal variance, and categorical variables were analyzed using the chi-squared contingency test. We assumed an alpha level of less than or equal to .05 to be significant.

RESULTS

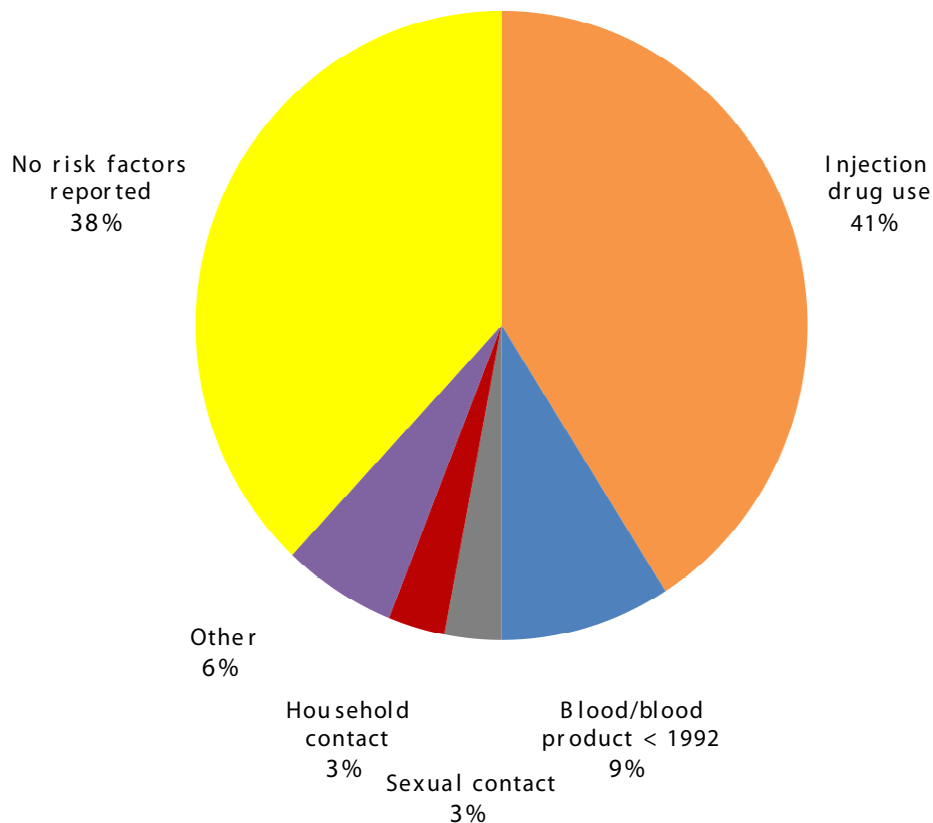
HCV Diagnostic Testing: We identified 35,712 unique patients ≥ 18 years of age at the beginning of the study period who had at least one in-patient admission(s) or out-patient visit(s) to an IHS facility in one of the two service units during the study period. An electronic medical records search yielded a total of 323 patients (1%) with at least one HCV-associated ICD-9 diagnosis. Of these patients, 30/323 (9.3%) had neither mention of hepatitis C in their chart nor any HCV testing and were judged to be coding errors. Paper charts were available and reviewed on 251/293 (86%) of charts without coding errors.

Among these 251 fully-reviewed patient charts, an HCV EIA was performed and recorded in 209 (83%). The remaining 42 (17%) patient charts mentioned HCV, but no diagnostic testing was recorded. Hepatitis C virus EIA was positive in 206/209 (99%). Hepatitis C virus past or present infection was confirmed in 144 (70%) of the 206 patients with a positive EIA: 94 (65%) by positive nucleic acid test (NAT) alone; 15 (10%) by positive recombinant immunoblot assay (RIBA) alone; and 35 (24%) by both RIBA and PCR. No patients had a positive EIA but negative confirmatory test. The rest of our analysis focused on the 144 patients with confirmed past or current HCV infection.

Demographics: Patients with confirmed past or current HCV infection were 54% male. Mean age was 41.8 years (95% CI, 40.0 – 43.6) as of the beginning of our study period 10/1/01). Mean age was 39.8 years among men and 42.4 years among women (t-test for means $p = .09$). Patients were affiliated with 57 different American Indian tribes.

Risk Factors: CV risk factor data were recorded in the charts of 90/144 (63%) confirmed patients, among whom the majority reported injection drug use (Figure 1).

Figure 1. Risk factors among 144 AI/AN patients with confirmed hepatitis C infection at two IHS service units, 2001-2003



Clinical Data: Clinical data are summarized in Table 1.

Table 1. Clinical Characteristics of 144 AI/AN Patients with Confirmed Hepatitis C Infection at Two IHS Service Units, 2001-2003

Characteristic	Result
Co-Morbid Medical Conditions	
Alcoholic liver disease	17/125 (14%)
Alcohol use ever	113/125 (90%)
Alcohol use documented when most recently asked	47/125 (38%)
Non-alcoholic steatohepatitis or non-alcoholic fatty liver disease	3/51 (6%)
Diabetes mellitus	21/136 (15%)
General Laboratory Testing	
Alanine transaminase, IU/L (n = 126)	Range 123 - 1313 IU/L; median 68 IU/L
Infectious Disease Testing	
HCV genotype	
1/1a/1b/1c	38/56 (68%)
2/2a/2b/2c	9/56 (16%)
3/3a/3b	8/56 (14%)
HCV RNA, IU/ml (n = 75)	Range 0 - 4,510,000 IU/ml; median 182,000 IU/ml
Co-infections:	
HIV	4/65 (6.2%)
HBV	
Total anti-core antibody	1/32 (3%)
IgM anti-core antibody	0/38 (0%)
HBV surface antibody (HBsAb)	13/71 (18%)
HBV surface antigen (HBsAg)	2/89 (2%)
Other Diagnostic Testing	
Liver ultrasound performed	31/144 (22%)
Liver CT performed	4/144 (3%)
Liver biopsy performed	17/144 (12%)
Vaccination	
Hepatitis A vaccination documented	43/142 (30%)
Hepatitis B vaccination documented	54/142 (38%)

Treatment: Initiation of combination therapy (ribavirin and interferon) for HCV infection was documented in 37/144 (26%) patients.

DISCUSSION

This is the first report of HCV diagnoses in a well-defined population of AI/ANs outside of Alaska to include information on hepatitis C treatment and follow-up,^{2,10-12} and points to several areas in which care for HCV-infected patients might be improved within the IHS healthcare delivery system in this region.

Our results confirm that an important co-morbidity associated with worse clinical outcomes in HCV-infected patients, alcohol use, was common in this AI/AN population. Expanded resources for alcohol counseling and treatment are critically needed in this population.

We found that risk factors were not documented in the charts of 38% of patients with confirmed HCV infection (Figure 1). A systematic, standardized approach to more complete risk factor assessment and documentation for all AI/AN patients seeking care in these settings would ensure that more high-risk patients are appropriately tested for HCV and receive risk reduction counseling.

We found many of the steps recommended in evaluation and follow up of HCV-antibody positive persons^{6,13} were not clearly documented, and thus modifications to clinical protocols for HCV-positive patients would be beneficial. First, we found that confirmatory HCV testing was not obtained in 30% of patients with a positive HCV EIA. In an additional 10% of patients, only RIBA was used to confirm HCV antibody presence, and no further test to distinguish past from current infection was documented. A standardized protocol to automatically perform confirmatory HCV testing on EIA-positive patients would help ensure diagnostic accuracy so that patients with current, active HCV infections receive appropriate care promptly and those that are HCV-RNA negative avoid unnecessary medical interventions.

Persons with confirmed current hepatitis C infection should be evaluated for the presence and extent of chronic liver disease. We found documentation of the recommended ALT test in 88% of patients, a quantitative HCV test in 52%, and genotype in 39%. Only 12% of patients had a documented liver biopsy, which is helpful in determining stage of chronic liver disease with presence of scarring.¹³ Similarly, our results indicate that testing for co-infections with HIV and HBV was incomplete. Since injection drug use, the most commonly documented risk factor in this and other HCV patient populations, is also a risk factor for HIV and HBV infection, it is important to test appropriately for these infections as well. Co-infection may dramatically affect the clinical course of HCV, as well as treatment options.^{13,14}

HCV treatment was documented to have been initiated in 37/144 (26%) patients. Hepatitis C treatment options for AI/AN people have increased, so treatment may have become more available since the time period included in our data set. Although currently recommended combination therapy with ribavirin and interferon is generally not available as standard treatment at most IHS facilities, treatment options for this population are enhanced by an ongoing collaboration between IHS and the University of New Mexico Health Sciences Center's Project ECHO (Extension for Community Healthcare Outcomes).^{15,16}

Lastly, vaccination against HAV and HBV was documented in only a minority of charts. Although our data may underestimate actual HAV/HBV immunization coverage in this population since patients may have been vaccinated elsewhere, the overall absence of documentation of HAV or HBV immunity is problematic, and immunization guidelines should be added to the protocols suggested above.

Limitations of this investigation include the fact that we established HCV infection diagnoses retrospectively based on ICD-9 coding, so patients with HCV infection had to be identified as such by the IHS health system to be counted. Therefore, our results are not a measure of the underlying

prevalence of HCV infection in the population, which is certain to be higher than the rate of diagnosed HCV infections that we found. Our investigation evaluated medical chart-documented diagnoses, and does not reflect the entirety of hepatitis C infection in the AI/AN population, which has well-documented disparities in CLD mortality.^{1,2} In addition, although using ICD-9 codes is a convenient and cost-effective method for looking at diagnoses in large populations, this approach is also subject to limitations, such as describing complex human diseases with a limited number of specific codes.^{17,18} Because we depended upon narrative chart notes to determine risk factors, data regarding risks for HCV infection are likely to be incomplete. Finally, this study is specific to patients accessing a single health care system and may not apply to other AI/AN and non-AI/AN populations and health systems.

CONCLUSIONS

In this population of 35,712 AI/AN adults using two IHS facilities, we identified by medical record review over 250 patients with possible, and 144 with confirmed, HCV infections. There were significant gaps in documentation of HCV-associated risk factors, laboratory confirmation of HCV infections, screening and testing for co-morbid conditions, vaccination, and recommended follow up for evaluation of chronic liver disease and possible treatment. Comprehensive management of HCV infections in this population with noted health disparities will require more standardized laboratory workup of both HCV and co-infections, improvements in risk factor ascertainment and documentation, and improved adult vaccination.

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.

Appendix A: Hepatitis C-associated ICD-9 Codes

571.4	Chronic hepatitis
571.40	Chronic hepatitis, unspecified
571.41	Chronic persistent hepatitis
571.49	Other chronic hepatitis: Active, aggressive recurrent hepatitis
Excludes: viral hepatitis (acute, chronic) (070.0-070.9)	
070.41	Acute or unspecified hepatitis C with hepatic coma
070.44	Chronic hepatitis C with coma
070.51	Acute or unspecified hepatitis C without hepatic coma
070.54	Chronic hepatitis C without hepatic coma

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ACKNOWLEDGEMENTS

The authors gratefully acknowledge the assistance of Donald Clark, MD, MPH; Joanna Buffington, MD, MPH; and the medical records technicians at the data collection sites.

Support

This work was conducted as part of the authors' normal duties at the University of New Mexico School of Medicine, the US Centers for Disease Control and Prevention, and the Indian Health Service. It required no separate funding.

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