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HIV Infection Status as a Predictor of Hepatitis C Virus RNA Testing in Primary Care

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Abstract

Introduction—Receipt of hepatitis C virus (HCV) RNA testing following a positive HCV antibody (anti-HCV+) test result to establish current infection is a quality indicator for HCV-related care. This study examines HIV infection status as a predictor of HCV RNA test receipt after an anti-HCV+ result in the primary care setting.

Methods—Electronic medical records of anti-HCV+ patients from a multisite retrospective study of patients aged ≥18 years who utilized one or more primary care outpatient services during 2005–2010 were analyzed in 2014. A multivariable logistic regression model examined the independent relationships between patient characteristics and receipt of HCV RNA testing.

Results—Among 1,115 anti-HCV+ patients, 133 (11.9%) were also HIV-positive. Of these, 77.4% (*n*=103) underwent HCV RNA testing to determine current infection status. By contrast, 66.7% (*n*=654/980) of anti-HCV+ patients who were HIV-negative received HCV RNA testing. Following multivariable adjustment, the odds of receiving HCV RNA testing were higher among anti-HCV+ patients who were also HIV-positive (AOR=1.9, 95% CI=1.2, 3.0), compared with their HIV-negative counterparts. Elevated alanine aminotransferase level was also associated with receipt of HCV RNA testing (AOR=1.9, 95% CI=1.4, 2.4). Black race was associated with decreased odds of receiving HCV RNA testing (AOR=0.7, 95% CI=0.5, 1.0).

Conclusions—HIV infection status is independently associated with the likelihood of receiving HCV RNA testing following an anti-HCV+ result. One quarter of anti-HCV+ patients who were also HIV-positive and one third of their HIV-negative counterparts, respectively, did not receive testing to establish active HCV infection, which is imperative for appropriate care and treatment.

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Introduction

An estimated 3.2 million people in the U.S. are currently infected with hepatitis C virus (HCV).[1,2] Approximately 10%–15% of those identified with HCV in the U.S. are also infected with HIV.[1,3–5] Individuals with HCV infection are at an elevated risk for cirrhosis, hepatocellular carcinoma (HCC), liver transplantation, and death.[6–9] HCV co-infection with HIV can exacerbate the expected natural history of HCV,[10–12] complicating management and treatment regimens, and accelerating progression to fibrosis, cirrhosis, and HCC.[13–15]

Antiviral treatment for HCV has been demonstrated to be effective among HCV/HIV co-infected people and can be used safely in concert with HIV antiretroviral therapy.[16] The benefits of HCV treatment, such as regression of liver fibrosis and decreased mortality, are observed in both mono- and co-infected individuals.[11]

Despite guidance for the management and treatment of people who are co-infected with HIV and HCV,[17–19] many do not receive the recommended quality of care,[16] and therefore are unable to initiate treatment or manage their infection, and experience a lower quality of life.[20,21] CDC recommends that all individuals who test positive for HCV antibodies (anti-HCV+) receive HCV RNA testing to establish current infection and facilitate receipt of appropriate care and treatment.[20,22] However, studies show that 24%–39% of patients do not receive HCV RNA testing after an anti-HCV+ test result.[22–25] Moreover, HCV/HIV co-infection is associated with greater odds of receiving high-quality care (e.g., receipt of HCV RNA testing for diagnosis of HCV viremia) than HCV infection alone.[22] A post hoc cross-sectional analysis was performed to examine HIV infection status as an independent predictor of receiving HCV RNA testing among primary care outpatients with an anti-HCV + test result.

Methods

Study Participants

Electronic medical record (EMR) data of anti-HCV+ patients identified from the BEST-C Retrospective Cohort Study[26] was used; BEST-C was designed to examine HCV testing and prevalence in four large health centers in the U.S.[26,27] Data collection was based on review of EMR data for new patients aged ≥18 years utilizing one or more primary care outpatient services between January 2005 and December 2010, who had no previous diagnosis of HCV infection. Of 209,076 patients in the cohort, 17,464 were tested for anti-HCV.[26] The current analysis was restricted to 1,115 anti-HCV+ patients.

Measures

The outcome measure was receipt of HCV RNA testing. HCV RNA testing was defined as receipt of HCV RNA testing following an anti-HCV+ test result. Independent patient characteristics examined included birth year, race/ethnicity, gender, marital status, history of injection drug use (IDU), history of elevated levels of alanine aminotransferase (ALT), and HIV infection status. HCV genotyping was also explored. (Definitions for IDU, ALT, and HIV infection are provided elsewhere.[26]) HCV genotyping data were derived from EMR laboratory data.

Statistical Analysis

Mean frequencies and percentages were calculated to describe the characteristics of the analytic population. A multivariable logistic regression model was fit to examine independent relationships between receipt of HCV RNA testing (dependent variable) and patient characteristics (HIV infection status, birth year, gender, marital status, race/ethnicity, history of IDU, and history of elevated ALT level, controlling for total number of visits). Statistical significance was set at a two-tailed *p*-value of 0.05. Data were analyzed using SUDAAN, version 11.0.0 and SAS, version 9.3; analyses were completed in 2014.

Results

Table 1 shows the characteristics of the 1,115 anti-HCV+ patients included in this analysis. Of these, 757 (67.9%) received HCV RNA testing to establish infection, of which 550 (72.6%) had positive results. Of those with positive RNA results, 389 (70.7%) received genotyping. Genotype 1 was most commonly identified (76.3%), followed by genotype 2 (8.7%), genotype 5 (5.9%), genotype 3 (4.9%), and genotype 4 (1.0%). Of all anti-HCV+ patients, 133 (11.9%) were identified as infected with HIV.

Among the 133 anti-HCV+ patients with positive HIV status, 77.4% (*n*=103) were tested for HCV RNA to establish HCV infection. By contrast, 66.7% (*n*=654/980) of anti-HCV+ patients with negative HIV status received HCV RNA testing. After multivariable adjustment, the odds of receiving HCV RNA testing were nearly twice as high among anti-HCV+ patients who were HIV infected compared with anti-HCV+ patients who were HIV negative (AOR=1.9, 95% CI=1.2, 3.0) (Table 2). Similarly, patients with a history of elevated ALT were almost twice as likely to receive HCV RNA testing (AOR=1.9, 95% CI=1.4, 2.4) compared with patients with normal/unknown ALT levels. Additionally, black race was marginally associated with decreased odds of receiving HCV RNA testing (AOR=0.7, 95% CI=0.5, 1.0). Gender, birth cohort, marital status, and IDU history were not independently associated with receipt of HCV RNA testing (Table 2).

Discussion

Testing for HCV RNA to determine active HCV infection is a necessary step to ensure accurate diagnosis of HCV and appropriate care and treatment for patients, especially given the availability of treatment with high cure rates.[16,28,29] This analysis indicates that anti-HCV+ patients who are also HIV positive are more likely to be tested for evidence of HCV viremia, compared with their HIV-negative counterparts. This finding may reflect routine clinical practice at the four healthcare systems from which patients were drawn for this study; it is reasonable to think that a physician with knowledge of a patient's HIV-positive status would be more aware of the importance of confirming active HCV-infection status in an anti-HCV+ patient, and therefore would be more likely to request HCV RNA testing.[22] HIV-positive patients are also more likely to be in the care of infectious disease specialists, who may be more likely to recommend HCV RNA testing to establish current infection and seek treatment.

The observation that patients with a history of elevated ALT levels have greater odds of receiving HCV RNA testing supports results from earlier studies,[22,24] and may be indicative of healthcare provider knowledge of the high correlation between persistently elevated ALT levels and the probability of liver disease.[17,30–32] The association between black race and lower odds of receiving HCV RNA testing may be confounded by lower levels of healthcare access among blacks[33,34] and should be interpreted with caution, in part owing to the inability to adjust for socioeconomic measures (e.g., insurance type).

Limitations

This study has several limitations. First, although HCV RNA testing is only one component of the continuum of care,[22,35] no data for other measures of HCV care were available. Second, data on history of blood transfusion, an important route of HCV transmission among older adults, were unavailable. Third, HCV RNA testing performed outside participating health systems may not have been captured. Fourth, cross-sectional analysis of the data limits the ability to assess temporal associations between independent risk factors and outcomes; for example, HIV testing may have occurred before or after HCV RNA testing. Finally, no distinction was made between current and past IDU. However, because of recall bias, past IDU (versus current use) is less likely to be reflected in an EMR.

Conclusions

These findings suggest that HIV infection status is independently associated with the likelihood of receiving HCV RNA testing following an anti-HCV+ test result. However, 26% of HIV-positive and 33% of HIV-negative patients did not receive HCV RNA testing to establish active HCV infection. HCV RNA testing following an anti-HCV+ result should be conducted for all anti-HCV+ people to facilitate access to appropriate care and treatment for those with active HCV infection.

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Table 1

Characteristics of HCV Antibody Positive Patients, 2005–2010

N=1,115	Number of patients, *n* (%) [a]
Age, median (IQR)	52 (45–57)
Birth cohort	
Born before 1945	90 (8.1)
Born 1945–1965	829 (74.3)
Born after 1965	196 (17.6)
Gender	
Male	686 (61.5)
Female	429 (38.5)
Marital status[b]	
Married	319 (28.6)
Widowed/divorced	164 (14.7)
Never married	632 (56.6)
Race/ethnicity[b]	
White	330 (29.6)
Black	574 (51.5)
Hispanic	129 (11.5)
Asian/Other	82 (7.4)
History of IDU	
Yes	361 (32.4)
No	754 (67.6)
Elevated ALT	
Yes	690 (61.9)
No	425 (38.1)
HIV Positive	
Yes	133 (11.9)
No	982 (88.1)

ALT, alanine aminotransferase; HCV, hepatitis C virus; IDU, injection drug use; IQR, interquartile range.

[a] Unless otherwise noted.

[b] Missing values for race/ethnicity(5.8%) and marital status (0.1%) were multiply imputed within the context of the larger dataset of 209,076 patients.[26]

Table 2

Association Between HIV-Infection and Receipt of HCV-RNA Testing Following a Positive HCV Antibody Test Result

N=1,115	AOR[a] (95% CI)	*p*-value
HIV positive		
Yes	1.7 (1.1, 2.8)	**<0.01**
No	1.0	—
Birth cohort		
Born 1965 or before	1.0	—
Born after 1965	1.3 (0.9, 1.9)	0.15
Gender		
Male	0.9 (0.7, 1.2)	0.57
Female	1.0	—
Marital status[b]		
Married	1.0	—
Widowed/divorced	0.8 (0.6, 1.3)	0.47
Never married	0.9 (0.6, 1.2)	0.37
Race/ethnicity[b]		
White	1.0	—
Black	0.7 (0.5, 1.0)	**<0.05**
Other	0.9 (0.6, 1.3)	0.47
History of IDU		
Yes	0.9 (0.7, 1.3)	0.68
No	1.0	—
Elevated ALT		
Yes	1.8 (1.4, 2.4)	**<0.001**
No	1.0	—

Note: Boldface indicates statistical significance ($p<0.05$).

ALT, alanine aminotransferase; HCV, hepatitis C virus; HCV-RNA, hepatitis C virus-ribonucleic acid; IDU, injection drug use.

[a] Logistic regression model adjusted for all variables shown in table plus total number of visits.

[b] Missing values for race/ethnicity (5.8%) and marital status (0.1%) were multiply imputed within the context of the larger dataset of 209,076 patients.[26]