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Patient and Provider Characteristics Associated with the Decision of HIV Coinfected Patients to Start Hepatitis C Treatment

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Abstract

Hepatitis C (HCV) and HIV coinfection is common and liver disease is a leading cause of morbidity and mortality among coinfected patients. Despite advances in HCV treatment, few HIV coinfected patients actually initiate treatment. We examined patient and provider characteristics associated with a patient's decision to accept or refuse HCV treatment once offered. We conducted patient chart abstraction and surveys with 127 HIV coinfected patients who were offered HCV treatment by their provider and surveys of their HCV care providers at three HIV clinics. Participants were mostly male (87%), minority (66%), and had a history of injection drug use (60%). Most had been diagnosed with HIV for several years ($X = 13.7$ years) and reported HIV transmission through unprotected sex (47%). Of the 127 patients, 79 accepted treatment. In multivariate analysis, patients who had a CD4 greater than 200 cells/mm^3 and a provider with more confidence about HCV treatment were more likely to accept the recommendation to start treatment; younger age was marginally associated with treatment acceptance. In bivariate analysis, added correlates of treatment acceptance included male gender, no recent drug use, and several provider attitudes regarding treatment and philosophy about determination of patient treatment readiness. Patient and provider characteristics are important when understanding a patient's decision to start or defer HCV treatment. Further research is needed to better understand barriers to treatment uptake as new and more effective HCV treatments will soon be available.

Introduction

Approximately 30% of HIV-positive individuals in the United States are coinfected with hepatitis C (HCV), including up to 90% of HIV-positive injection drug users (IDUs).[1,2] Liver disease is a leading cause of mortality in this population.[3–5] Although the current standard of care for HCV treatment, pegylated-interferon (PEG-IFN) and ribavirin (RBV), can be curative in approximately 20–50% of HIV coinfected patients,[6–9] studies consistently show that a minority of coinfected patients are evaluated for treatment,[10] that less than one third of such patients in the United States are deemed eligible for HCV treatment, and less than 10% actually receive treatment.[11–16] Furthermore, while patients are eligible for treatment, they often do not receive treatment until 1–2 years later.[10] Several barriers may contribute to the low treatment uptake including factors related to both providers and patients.

The provider has an important role in whether a patient pursues HCV treatment, as the provider must first recommend or offer treatment to the patient. Some research suggests that provider attitudes (e.g., perceived treatment need and effectiveness; views about substance use and mental health as impediments to treatment readiness) affect rates of both provider treatment recommendation and patient uptake of treatment.[17] Provider attitudes about treatment can influence how they recommend and discuss treatment options with their patients, which in turn may influence the patient's decision to start or defer treatment. Providers that recommend treatment with more urgency, and are perceived as

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trustworthy, nonjudgmental, and accepting are associated with patient decisions to start treatment.[18–22]

Once the provider offers treatment, the patient ultimately makes the decision to initiate or defer treatment, and 15%–30% of coinfected patients decide to decline treatment.[12–14] Clearly, many patients perceive the risks of treatment to outweigh its benefits,[19] although few studies have examined specifically how coinfected patients make HCV treatment decisions. A patient's willingness to undergo HCV treatment is likely influenced by how the patient views both the efficacy and the burden or risk of treatment. Many patients do not understand that HCV treatment can be curative,[22] and patients commonly fear the side effects of HCV treatment and its impact on their quality of life and functioning,[22,24–26] as PEG-IFN/RBV is considered to be highly toxic with side effects that include flu-like symptoms, fatigue, depression, and hematologic abnormalities.[27–30]

Psychosocial functioning may also contribute to a patient's treatment decisions. Active mental health and substance abuse problems are often viewed by providers as treatment contraindications,[12,13] partly because substance use can worsen liver disease[31] and treatment side effects can result in depression, psychiatric deterioration and relapse into drug use.[27,30] The emphasis that providers place on mental health stability and abstinence from substance use may subsequently increase the self-awareness of patients with regard to their psychosocial readiness for treatment.[32]

With PEG-IFN/RBV having been shown to have some effectiveness, and improved treatment options apparently on the horizon,[4] more research is needed on the factors that influence the HCV treatment decisions of patients. In this article we report findings from an analysis of provider and patient factors associated with whether or not a patient decides to accept HCV treatment once it has been recommended by their provider.

Methods

Setting

The study was conducted at three HIV clinics in Los Angeles. The participating clinics were located at the Greater Los Angeles Veterans Administration (VA) Medical Center, Harbor-UCLA Medical Center, and AIDS Healthcare Foundation (AHF). The sites differ on a number of characteristics including the number of HIV patients (400–1700) and HIV/HCV coinfected patients (100–650), involvement of a liver specialist (at only one site), and HCV treatment rates (10–40% of coinfected patients have received treatment). Although two of the sites are located within a larger medical center, the patients at each of the three sites receive their HCV care at the HIV clinic.

Sample

Patients. All clinic patients who were HIV/HCV coinfected, age 18 or older, and English speaking were eligible to participate. During the 4-month study enrollment period, the study coordinator at each site performed a clinical chart review of all patients attending the clinic for a routine visit to identify those who were coinfected with HCV and otherwise eligible. Patients were informed of the study while they were waiting to be seen by their provider; those who were interested in participating provided signed informed consent. Although we did not keep a systematic record of patient refusals to participate, the site coordinators report that very few patients opted not to participate. Only data from participants whose provider had recommended that they start HCV treatment after a complete medical work-up were included in the analyses reported in this article.

Providers. All providers at each site who manage HCV care of coinfected patients and make decisions about HCV treatment were asked to complete a survey. Providers were paid $50 for completing the survey, except at the VA where institutional regulations did not allow any payment.

The study protocol was approved by the Institutional Review Board at RAND and the individual clinics.

Measures

From patient medical charts, we abstracted data related to HIV and HCV disease characteristics, and psychosocial functioning. For patients who had initiated HCV treatment, data were abstracted that were closest and prior to the date HCV treatment was started; for patients who had been offered but had thus far chosen not to start treatment, data closest to study enrollment were abstracted as these represent the latest indicators upon which the patient was deciding not to start treatment. Patient demographic and background characteristics were obtained with patient surveys at time of study enrollment. Among providers, we examined beliefs and philosophies about HCV management and treatment, and characteristics of their training and clinical practice, which were assessed with surveys of providers at the time of study enrollment.

Patient measures

HCV treatment status. Treatment status was abstracted from the clinic charts by first determining whether the patient had ever been offered treatment, and among those who had been offered, whether or not the patient had accepted or refused treatment.

Demographic and background characteristics. Variables that were assessed included self-reported age, gender, race/ethnicity, education, employment, and relationship status. Participants were also asked the approximate date in which they were diagnosed with HIV and HCV, and how long they have attended the clinic.

HCV/HIV disease characteristics. Stability of HIV was assessed with CD4 cell count, HIV viral load, and whether or not the patient was on HIV antiretroviral therapy. HCV viral load and genotype were also measured. Variables were converted to dichotomous variables based on clinical significance (e.g., CD4 count, ≤ 200 cells/mm^3; HIV viral load, ≤ 400 copies per milliliter; and genotype 1 or 4 versus 2 or 3).

Psychosocial functioning. We extracted from chart data whether the patient had a diagnosis of depression, any other psychiatric disorder, or problems with use of alcohol and illicit drugs in the prior 6 months. We also extracted whether the patient was receiving any form of psychiatric treatment (e.g., psychotropic medication, counseling).

Provider measures

Medical practice and training characteristics. These variables included training discipline (e.g., physician, nurse practitioner, physician's assistant), number of years practicing at the clinic, number of HIV/HCV coinfected patients cared for, and number of patients treated with interferon and ribavirin.

Perceived confidence in HCV care management. This measure was developed for the study and assessed the level of confidence providers had with five aspects of HCV management: overall management of HCV in HIV coinfected patients, HCV treatment in HIV coinfected patients, side effects of HCV treatment, HCV treatment for patients with substance abuse, and HCV treatment for patients with mental health problems. Each item was rated on a 5-point Likert scale ranging from "not confident" to "very confident" ($\alpha = 0.96$). Mean item score was calculated and higher scores represent more confidence in HCV care management.

Treatment outcome expectations. This measure was adapted from Meredith et al.[33]; five items assessed the perceived likelihood that HCV treatment would be effective in achieving the following five specific goals: improving patient's functioning, minimizing treatment side effects, preventing liver failure and disease progression, relieving acute liver symptoms, and alleviating pain and suffering. Each item was rated on a 5-point Likert scale ranging from "very likely" to "very unlikely" ($\alpha = 0.84$). Mean item score was calculated and higher scores represent a greater likelihood that HCV treatment would be effective in obtaining these goals.

Provider philosophy regarding patient psychosocial treatment readiness. Provider philosophy regarding assessment of patient readiness for HCV treatment was assessed by asking the provider, in separate questions, about their approach to treatment if a patient reported (1) current drug use, (2) current alcohol use, and (3) moderate depression but was otherwise a good HCV treatment candidate. Response options consisted of five scenarios that ranged from deferring treatment until the condition (drug use, alcohol use, depression) was treated and in remission for a good period of time to counseling the patient about the risks of the condition for HCV treatment but letting the patient decide whether or not to start or defer treatment.

Data analysis

Descriptive statistics were used to examine the response distributions of variables. Bivariate statistics (independent two-tailed *t*-tests, χ^2 tests) were used to assess the correlates of whether or not the patient accepted the recommendation to start HCV treatment. A logistic regression model of complete cases was then used to examine predictors of the patient decision to accept or refuse treatment. To maintain an adequate ratio of the number of observations in each group to the number of predictors, we used a parsimonious regression model with 6 predictors,[34] which yielded a ratio of 7 observations per variable in the smaller group (treatment refused), and 12 observations per variable in the larger group (treatment accepted). From among the variables that were associated with the patient decision to accept or refuse treatment at the $p < 0.05$ level of significance in the bivariate analysis, we selected 6 variables that represented each of the predictor domains (i.e., patient demographics, HIV/HCV disease indicators, psychosocial readiness, and provider characteristics). Finally, to account for potential correlations among outcomes of patients in the same clinic that share a provider, we computed robust standard errors for the regression model to account for intracluster correlations within provider.

Results

Sample description

A sample of 173 patients enrolled in the study, of whom 127 (73%) had been recommended HCV treatment by their provider, and it is this subsample that serves as the dataset for the analyses reported in this paper. Most (87%) participants were male, mean age was 49.4 (standard deviation [SD] = 9.0), 58% had at least some college education, 66% were racial/ethnic minorities (including 36% who were African American and 21% who were Hispanic), 41% identified as heterosexual, and 60% had a history of injection drug use. Of the heterosexual sample, 32% reported HIV transmission through shared intravenous needles and 29% through unprotected sex compared to 8% and 60% of those who indicated homosexuality or bisexuality as their sexual orientation, respectively. Most participants had been diagnosed with HIV for several years ($X = 13.7$ years), and had been receiving care from the study site for an average of 8.5 years. Mean time since HCV diagnosis was 7.8 years, and 76% had an HCV genotype of 1 or 4.

Fourteen primary HCV care providers completed the survey, accounting for the HCV care providers of 115 (91%) of the patient participants who had been offered treatment. The 12 patients with missing provider data were missing at random and were not different from the remaining 115. Among the 14 providers surveyed, half were male, 57% were Caucasian, and 69% were physicians. Providers had between 2 and 19 years experience at the current clinic ($X = 11.1$ years, SD = 6.1) and the number of co-infected patients that each provider had treated with interferon-based therapy ranged from 4 to 60 ($X = 21$; SD = 19).

Bivariate analysis of variables associated with HCV treatment acceptance

Of the 127 patients who were offered HCV treatment, 79 (62%) decided to start HCV treatment, while the other 48 (38%) refused treatment. For those who had been offered treatment, this event took place an average of 6.2 years (SD = 5.8 years; range, 1 week to 23.0 years) after HCV diagnosis and 2.3 years (SD = 2.7 years; range, 1 week to 10.9 years) prior to the study survey. The proportions of patients offered treatment at each site, who then accepted treatment, were statistically similar across sites with rates ranging from 67% (46/69) at AHF and 65% (15/23) at Harbor, to 51% (18/35) at the VA.

Compared to those that refused treatment, patients who accepted treatment were more likely to be younger, male, have CD4 counts above 200 cells/mm^3, and no recent illicit drug use (Table 1); there was also a trend for African Americans to be less likely to accept treatment when recommended. With regard to provider characteristics, patients who

Table 1. Bivariate Correlates of Patient Acceptance of Hepatitis C Virus Treatment

	Treatment accepted (n = 79)	*Treatment refused (n = 48)*
Patient demographics		
Male gender[a]	92%	77%
African American[b]	30%	46%
Mean age[a] (years)	48.1	51.2
Employed	37%	25%
Any college education	57%	58%
Currently in a relationship	26%	17%
HIV and HCV disease characteristics		
Mean CD4 count[c] (mm^3)	533	410
CD4 count ≤ 200[c]	1%	21%
Mean log_{10} HIV RNA (copies/mL)	2.24	2.17
HIV RNA ≤ 400	79%	83%
On ART	91%	96%
HCV genotype 1 or 4	72%	81%
Mean log_{10} HCV RNA (copies/mL)	6.09	6.24
Psychosocial functioning		
Depression (past 6 months)	39%	44%
Other psychiatric disorder (past 6 months)	24%	20.8%
Frequent alcohol use (past 6 months)	8%	15%
Illicit drug use (past 6 months)[a]	11%	27%
Mean ART adherence	92%	87%
Any missed ART doses (past week)	23%	33%
Any missed clinic appointments (past 6 months)	34%	33%
Provider characteristics		
Number of coinfected patients[c]	309.6	132.0
Number of patients treated with IFN/RBV[b]	43.8	34.9
Treat with small amounts of alcohol is okay[c]	45%	19%
Treat only if patient's drug use stopped	44%	57%
Treat only if patient's depression is in remission[a]	48%	64%
Confidence to treat HCV[c]	3.4	2.9
HCV treatment outcome expectations[a]	4.3	4.0

[a] $p < 0.05$.
[b] $p < 0.10$.
[c] $p < 0.01$.
HCV, hepatitis C virus; ART, antiretroviral therapy; IFN/RBV, interferon/ribavirin.

accepted treatment were more likely to be seen by providers with higher caseloads of HCV coinfected patients, more lenient views about depression and alcohol use as barriers to HCV treatment readiness, more confidence in their HCV care management skills, and more positive HCV treatment outcome expectancies (Table 1); having a provider who had treated more patients with PEG-IFN/RBV was marginally associated with treatment acceptance.

Table 2. Characteristics Associated with Patient Acceptance of HCV Treatments in Multivariate Analysis ($n = 127$)

	Decision to accept treatment O.R. (95% C.I.)
Patient variables	
Age	0.95 (0.91, 0.99)[a]
CD4 count ≤ 200	0.08 (0.01, 0.40)[b]
Illicit drug use in past 6 months	0.65 (0.18, 2.33)
Provider variables	
Confidence to treat HCV	2.19 (1.35, 3.56)[b]
Treat only if patient's depression is in remission	0.70 (0.40, 1.20)
HCV treatment outcome expectations	0.69 (0.36, 1.33)

[a] $p < 0.05$, [b] $p < 0.01$; O.R., odds ratio; C.I., confidence interval.

Multivariate analysis of variables associated with HCV treatment acceptance

The six variables selected for inclusion in the logistic regression analysis consisted of the patient's age, whether the patient had a CD4 ≤ 200 cells/mm^3 and illicit drug use or depression, and provider variables including their views about providing HCV treatment to patients with depression, their level of confidence in HCV care management, and their treatment outcome expectations. Results showed that patients with CD4 counts at or above 200 cells/mm^3, and whose provider had more confidence about HCV treatment were found to be more likely to have accepted the recommendation to start HCV treatment (Table 2). Younger patient age was marginally associated with accepting treatment.

Discussion

Consistent with previous research,[12–14] almost 40% of the HIV coinfected patients in this study who were offered HCV treatment refused to start. This finding highlights the importance of understanding the factors that impact a patient's decision to start or defer treatment, given that liver disease is a leading cause of morbidity and mortality in this population and that promising, more effective HCV treatments will soon be available in the near future.[35]

Our multivariate analysis revealed that HIV stability was among the strongest predictors of treatment acceptance in this sample. Patients who had higher CD4 counts were more likely to start treatment. These results may allude to the need for HIV stability and a sufficiently intact immune system as a priority for initiation of treatment. HCV treatment guidelines state that while patients with lower CD4 can be treated,[7] higher CD4 counts are preferable because a temporary decrease of CD4 cells occurs during the course of treatment[4,36] and may render patients vulnerable to opportunistic infections.

Psychosocial indicators of patient treatment readiness, such as mental health and substance use have been shown to be associated with HCV treatment eligibility in several

studies,[13,37] suggesting their importance to provider assessments of treatment readiness, but these constructs were less influential to patients in this study. In bivariate analysis, patients who had no illicit drug use were more likely to accept treatment than patients with current drug use, indicating that current drug use plays a role in patients' assessment of treatment readiness; however, there was no evidence that alcohol use or depression had any influence on a patient's decision to accept or defer treatment.

Several provider characteristics were associated with patients' treatment decisions in bivariate analyses. Patients who accepted treatment had providers with more exposure to coinfected patients. These providers had larger coinfected patient caseloads and had treated more patients with PEG-IFN/RBV than providers of patients who declined treatment. Patients who accepted treatment were also matched with providers with more confidence in HCV care management, positive expectancies of HCV treatment, and were more lenient in their views about alcohol and depression in their treatment philosophies. Collectively, these results seem to suggest that patients tend to accept treatment more when matched with providers who have more contact with coinfected patients, more confident and hopeful views about HCV treatment, and flexibility with regard to the types of patients who could benefit from treatment. This finding highlights the importance of the patient and provider relationship.[21,23] These providers may project attitudes about HCV treatment that lead patients to feel more confident and hopeful about their ability to tolerate and benefit from HCV treatment.

The primary limitation of the study findings is the largely retrospective nature of the study design, and associated reliance on available chart abstracted data. The data from the supplementary self-report surveys conducted at study entry may not be reflective of the conditions present when treatment was offered. A prospective design that measured variables at the time the treatment decision was actually made would be optimal, but such a design was not feasible in terms of time and resources. Also, the findings cannot be considered generalizable to all coinfected patients, although nearly all coinfected patients who attended the clinic during the study enrollment period did participate.

Despite recommendations from providers to start HCV treatment, these data suggest that many patients defer or decline treatment once offered. Both provider and patient characteristics play a significant role in a patient's decision to start treatment. As newer and more efficacious (but perhaps even more burdensome) treatments are soon to be available,[4] it is unknown how these advances will affect patient treatment decision making. Therefore, it is important to continue to evaluate the barriers to treatment uptake so as to improve the quality of HCV care received by patients with HIV and HCV coinfection.

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Author Disclosure Statement

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